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A SYMPOSIUM ON
HODGKIN'S DISEASE*
BASED ON A SERIES OF 960
CASES DIAGNOSED CLINICALLY

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WHY THOMAS HODGKIN failed to receive an appointment in the Department of Medicine at Guy's Hospital is not known. The slightly older Bright and Addison, already members of the medical staff, would not be expected to have cast a vote against another good Edinburgh man even had they known that his star would shine as brightly as their own. Possibly some tyrant on the board of governors did not approve of his being a Quaker or his being careless in collecting fees — or perhaps there was some simpler explanation such as a dominant matron's disapproval of confirmed bachelorhood. Most certainly it was not related to any lack of accomplishment in his ten years of lecturing in the Department of Pathology, because during this period he had, among other things, become quite familiar with acute appendicitis and its complications, described aortic insufficiency three years before Corrigan, and in 1832 presented a paper to the Medico-Chirurgical Society of London¹ in which he was "induced to forward a few cases in which morbid alterations in structure observed in the course of cadaveric inspection had, so far as [he] was aware, not previously been made the subject of special attention. Joseph Sinnot, a child of nine, had been much reduced by an illness of about nine months during which he had been subject to pain in the back extending around to the abdomen. His belly was much distended with ascites and he had also effusion into the prepuce and scrotum. Ellenborough King, aged 10, and under the care of Dr. Bright, had been healthy until about 13 months ago when his strength,

flesh and healthy appearance began to fail. A tumour was observed in the left hypochondrium in the situation of the spleen and the glandulæ concatenatæ on the right side were observed to be considerably enlarged." Then followed the "appearances of the absorbent glands and spleen", the morbid entity which his colleague Sir Richard Wilks, in 1865, called "Hodgkin's disease", a condition which remains as poorly understood as Hodgkin's personality itself.

ETIOLOGY

It seems fair to say that little progress has been made in our understanding of the nature and cause of Hodgkin's disease. Many pathologists consider it to be a neoplasm, but, as Anderson² states, "it is difficult to conceive of a neoplasm in which the tumour cells are of so many different types, yet one which does not belong to the category of 'mixed' tumours". Others consider it to be a member of the granulomatous diseases — a poorly defined granulomatous pattern on which is superimposed a chronic inflammatory cell response — inferring a group relationship at least with such entities as tuberculosis, brucellosis, and protozoal and fungal infections.

The arguments in favour of a tuberculous etiology began in 1898 when Sternberg, like Hodgkin, described cases complicated by tuberculosis. These arguments continued without abatement until the publication in 1933 of L'Espérance, who championed the avian strain of tubercle bacilli. The weight of evidence against a tuberculous etiology is greater than that supporting it. A significant percentage of patients with Hodgkin's disease are anergic to tuberculin, and Medlar has shown that the disease is no more prevalent in proven tuberculous patients than in the normal population. When these two diseases do coexist in the same individual, each is separately identifiable on the basis of a characteristic cellular reaction, and, as pointed out by Jackson and Parker,³ it would be surprising if the same host, at the same time and at the same site, were to react in two distinct ways to a single etiological agent.

The bacillus of tuberculosis, of course, is only one of a number of infective agents implicated in a series of repeated cycles as the infective agent in

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Hodgkin's disease. Organisms of the brucella group, championed by Parsons and his group, have had their day, as have diphtheroid bacilli, *B. melitensis* and even amoebæ. These and *Cryptococcus hominis* seem to be no more than an accidental association with Hodgkin's disease. Some years ago Gordon⁴ showed that an extract of a lymph node of Hodgkin's disease when injected intracerebrally in the guinea-pig would cause, within 10 days, a fatal encephalitis in 60-65% of the animals. Subsequently, it has been shown that the common factor was the eosinophil and, in turn, probably one of its specific enzyme components. In any event, the test is of no more practical value than the finding of eosinophils in tissue involved by Hodgkin's disease.

Following inoculation with cell-free filtrates from Hodgkin's tissue there has been identification in tissue culture⁵ and chick embryos⁶ of intracytoplasmic inclusions having some of the characteristics of elementary bodies. Bostick thinks that he has isolated the agent responsible, but freely admits that he has a tiger by the tail in that proof is difficult to obtain. No animal develops Hodgkin's disease spontaneously nor can it be produced by transfer or culture. The production of paralysis in mice, mutations in *Drosophila* and specific alterations in tissue culture can at best add only to indirect evidence.

In expressing his own opinions on the nature and etiology of Hodgkin's disease, the first speaker in this symposium⁷ straddled the fence of uncertainty and planted his feet firmly on the ground of two good but quite different pastures. "The paragranuloma and the Hodgkin's granuloma on the basis of morphology at least are, albeit somewhat tenuously, compatible with an inflammatory etiology, while the appearance of Hodgkin's sarcoma on such a background can have no other interpretation than the progression of an inflammatory lesion to frank neoplasia."

SOME HÆMATOLOGICAL AND BIOCHEMICAL FEATURES

It has already been pointed out that Thomas Hodgkin was a pathologist and that his original description of the disease was in the nature of a pathological report. Now, 125 years later, the precise diagnosis of Hodgkin's disease remains the responsibility of the pathologist, more specifically in the domain of histopathology. Variations in blood morphology and blood biochemistry have been observed, but none is specific for the disease.

Some understanding of the hæmatological features of Hodgkin's disease is of importance in the management of particular patients. The mild or moderate degree of normocytic, normochromic anæmia found in about half the patients before treatment is difficult to explain in its entirety. One factor is that of shortened red cell survival, but this alone is usually not of sufficient degree to result in

anæmia if the marrow is functioning normally. Iron is available but not readily utilized and hæmatinics are of no value. Frequently, a more acute hæmolytic process may be precipitated by an auto-immune mechanism whereby the patient's own red cells are attacked by antibodies made by the patient himself. Whether the patient's red cells are themselves abnormal and incite the production of antibodies or whether the phenomenon is but a manifestation of the patient's ability to make abnormal serum proteins is not known. These patients present the usual clinical features of hæmolytic anæmia. The choice of ACTH, steroids, or splenectomy in the management of acute or sub-acute hæmolysis will depend on a consideration of all factors in the individual case.⁸ In a small number of patients anæmia of the myelophthisic type may follow upon the widespread infiltration of marrow by Hodgkin's disease. Treatment by radiation and chemotherapy can also be factors in the production of anæmia.

In about half of the patients with Hodgkin's disease the total white cell count is found to be above normal. In a few cases there will be leukopenia. Monocytosis with lymphocytopenia is a common finding. In the 10% of cases in which eosinophilia is observed the skin is often involved.

Thrombocytopenia may occur as a complication of splenomegaly. It may be associated with marrow failure as part of the disease process or may be a complication of treatment. The mechanism of thrombocytopenia in the presence of splenomegaly is not clearly understood, but the enlarged spleen is thought to suppress either production of platelets or their release from the marrow, or perhaps to phagocytize avidly the affected cells.

The sedimentation rate in Hodgkin's disease is usually elevated and is useful clinically as an index of activity of the disease.

The place of marrow aspiration in the diagnosis of Hodgkin's disease has received increasing attention in recent years. In a small number of cases it may be the only way of making a diagnosis. Varadi⁹ recommends that aspiration be done through points of bone tenderness. The practical problem is that of differentiating Reed-Sternberg cells from megakaryocytes. The differences cited are that the Reed-Sternberg cell has a very large nucleolus and sometimes nucleoli. Megakaryocytes, on the other hand, usually have no nucleoli or if present are very small. Furthermore, the cytoplasm of Reed-Sternberg cells is either nongranular or not nearly so granular as the cytoplasm of megakaryocytes. It has been reported also¹⁰ that Reed-Sternberg cells will not stain with periodic-acid Schiff stain whereas megakaryocytes will.

Most patients with Hodgkin's disease, at some stage of their disease, show alterations in serum proteins as demonstrated by either the Tiselius method or by paper electrophoresis. Arends¹¹ has pointed out that these changes are non-specific and include mainly an increase in α_1 , α_2 and/or β

globulin fractions. Sunderman and Sunderman,¹² using paper electrophoresis, suggest that the characteristic pattern for Hodgkin's disease is a decrease in total albumin with increases in α_1 , α_2 and γ -globulin.

TREATMENT

In his original paper Hodgkin referred to glands which had been reduced in size by previous treatment. What this treatment may have been is not stated. There is no doubt that nodes, especially in the neck area, may periodically enlarge and regress without specific treatment. The first mention of the use of Fowler's solution (sodium arsenite) was by Lissauer in 1865,¹³ but others had perhaps used this agent previously.

Surgery:

The radiosensitivity of Hodgkin's tissue and the propensity of the disease to behave as one of multicentric origin are sufficient reasons for most surgeons to leave the care of these patients to the radiotherapist. Exceptions are those cases where the disease may involve the gastro-intestinal tract or bone, requiring resection or other measures.

Radiotherapy:

Since the advent of x-rays about 60 years ago there have been progressive refinements in apparatus from the mechanical rectifiers operating at 150 K.V.P. through conventional high voltage into the supervoltage and cobalt-60 range of 2 to 3 MeV. energies. It has become relatively easy to deliver more adequate dosage with less discomfort to the patient. Almost all radiotherapists in this province accept the hope that the disease may be restrained and life prolonged by applying high dosage to localized masses, and have utilized the many theoretical advantages offered by the progress of physics. A much smaller school assumes that the disease will ultimately win any struggle and uses radiation in dosage sufficient only to relieve distressing symptoms.

In commenting on problems associated with the radiotherapy of Hodgkin's disease, Smith¹⁴ raises a point pertinent to these opposing schools: "What is the lethal dosage for tissue exhibiting the features of Hodgkin's disease?" Experienced radiotherapists have all observed that in the same patient the same dose may produce quite different responses in different regions, and that at one site the disease may never recur whereas at another it may reappear within a few months. The studies of Lenz, Wells and Stout with dosage effectiveness in lymphosarcoma are perhaps not applicable to Hodgkin's disease but in their series the recurrence rate of local disease clearly was inversely related to tumour dose.¹⁵ Smith himself feels that the dosage of initial treatment must be ample and protracted to and well beyond 3000 r if tolerated regionally

and systemically. The methods of attaining such dosage with due consideration for adjoining areas are defined in this report.

Generally advocated are (a) a rigorous initial radiotherapeutic approach to the regional adenopathy in the paraganuloma and granuloma group with heavy irradiation to the adjacent gland-bearing areas, and (b) the early recognition of symptoms and signs of disseminating disease with administration of appropriate treatment. This last is an urgent matter from the standpoint of achieving the best palliation.

Radiotherapists generally have an open mind concerning the value of prophylactic irradiation to areas not clinically involved by disease—a point discussed in detail by Peters.¹⁶

Chemotherapy:

As mentioned, Fowler's solution made its appearance about one hundred years ago. Those who have had considerable experience with it have expressed the opinion that its effect is not so marked in Hodgkin's disease as in leukæmia. Reduction in the size of glands does sometimes occur, but the results are of much shorter duration and much less satisfactory than those following radiation. For these reasons the chemotherapy of Hodgkin's disease did not attain any really useful status until the first of the alkylating agents appeared on the scene during the recent war.

As inferred from the above discussion, radiotherapy remains in this province the sheet-anchor of treatment for Hodgkin's disease, agents such as nitrogen mustard (methyl-bis (β -chloroethyl) amine) being reserved for cases where the extent of disease makes radiotherapy impracticable or where radiotherapy seems to have no further useful part to play in the management of the disease. It seems wrong to use an agent like nitrogen mustard initially in the treatment of any patient presenting with localized disease. Certainly, with nitrogen mustard or TEM (2,4,6-triethylenimino-s-triazine) given intravenously, a partial and in some cases complete disappearance of nodes may follow, but with almost equal certainty recurrence of growth in the same area will take place weeks or some months later. The whole body, so to speak, has been treated by a noxious agent behaving like x-rays when it is necessary to treat only a localized area. In the same patient adequate radiotherapy will, except in rare cases, cause complete regression of disease, and recurrence will seldom make its appearance in the same site.

At one or other of the various centres in Ontario the newer chemotherapeutic agents have been assessed as they have appeared. It seems general experience that only the alkylating agents seem to have a specific effect on Hodgkin's disease. ACTH and the adrenocortical steroids may in some cases improve appetite and sense of well-being but do not alter the course of the disease. A point of

practical interest is that nitrogen mustard remains the most reliable of the alkylating agents. TEM, when used intravenously, has the advantage of causing less nausea and vomiting than nitrogen mustard, but its effects are not so consistent. Remissions up to a year in length have been observed in a small number of cases following the use of nitrogen mustard or TEM. Recently, favourable remissions have been noted in a few patients with systemic disease using Leukeran (p-N,N-di(β -chloroethyl)aminophenylbutyric acid) orally in a dosage of 12 to 16 mg. daily for three to four weeks followed by a daily maintenance dose of 2 to 4 mg.

There is a place and time in the management of Hodgkin's disease for both radiotherapy and chemotherapy. Their efficient use depends upon a knowledge of the natural history of the disease and the usefulness and limitations of each form of therapy.

HODGKIN'S DISEASE IN CHILDREN

On the basis of clinical experience with 42 cases observed at the Hospital for Sick Children it would seem that the onset, course and response to treatment of Hodgkin's disease in children are similar to those in adults. However, involvement of the gastro-intestinal tract, central nervous system and skin has not been observed.

Enlargement of neck glands was the initial complaint in 29 of 40 cases. One-third of these patients had symptoms for over a year.

Ten out of 30 patients at risk survived five years. Five out of 22 patients at risk survived ten years.

THE PROBLEM

The annual volume of deaths assigned to Hodgkin's disease in the province of Ontario is relatively small. Since 1950, the number of recorded deaths has been around 80 per year. During the five years 1952-56, 399 deaths were assigned to Hodgkin's disease. This is 1.14% of all cancer deaths and about two out of every one thousand deaths from all causes during the period. Of these deaths 30% were in persons under 35 years of age. The sex ratio for deaths was 1.66 males to 1 female.

An unknown proportion of all patients with Hodgkin's disease in Ontario—possibly as great as two-thirds—are admitted to the regional cancer clinics of the Ontario Cancer Treatment and Research Foundation for diagnosis and/or treatment. From 1952 through 1956, 323 new cases of Hodgkin's disease were treated at the eight Ontario cancer clinics. This is 1.36% of the 23,813 new cases of malignant disease treated at the clinics during that period.

MATERIAL AND METHODS

This review is based on data recorded on the standard follow-up cards maintained by the eight regional cancer treatment clinics in Ontario from 1932 up to and including the year 1951. Two

TABLE I.—CLINICAL STAGE CLASSIFICATION OF HODGKIN'S DISEASE

Stage	Definition
I	Involvement of a single site or lymphatic region.
II	Involvement of two or more proximal (adjacent) lymphatic regions. A—with no symptoms of generalized disease. B—with symptoms of generalized disease.
III	Involvement of two or more distant lymphatic regions.

supplementary facts were secured for the special purposes of this conference: the findings of a review of all available tissue sections and a clinical classification or "staging" for each case, according to an agreed method (Peters)¹⁷ (Table I).

The analysis included 960 patients diagnosed clinically as having Hodgkin's disease. In order to avoid duplication in the overall analysis, 32 cases registered at two clinics were arbitrarily assigned to the first clinic at which they registered.

Of the 960 patients, 849 or 88.4% were registered at the clinics during the 14-year period 1938-1951. During this period a total of 940 deaths in Ontario were assigned to Hodgkin's disease, giving a case:death ratio of 0.90.

MICROSCOPIC CONFIRMATION

Out of the 960 cases included in the study, the diagnosis of Hodgkin's disease was confirmed histologically in 730, or 76.1%. No tissue was available for study in 141, or 14.7% of the cases.

All tissue sections on file at the clinics for the cases included in this study, including those not confirmed as Hodgkin's disease by the clinic pathologist, were sent to an agreed central point for review by one pathologist. Five hundred and ninety-one sections were available for this review. Table II gives the details of original and review pathological diagnosis.

It is of interest that of the 230 cases of Hodgkin's disease which had been confirmed at the clinics, slides relating to 547 or 74.9% were available for review. Of these cases, 422 or 77.1% were "re-confirmed" as being Hodgkin's disease. In 65 cases the reviewing pathologist was not prepared to call the disease Hodgkin's disease but did place it within the "malignant lymphoma" group. Twelve were considered to be cases of malignant disease of other sites. Twelve he considered non-malignant, and in 36 he was either unable or unwilling to make a diagnosis. On the surface this may seem like only a fair degree of correlation, but those familiar with the difficulties of interpretation of tissue of this type may agree that any comparable review of such a large number of cases would probably reveal the same degree of disparity of opinion.

AGE AND SEX DISTRIBUTION OF CASES

Of the 422 reconfirmed cases, only 23 persons were under 15 years of age while 188 were under 35 years of age (Table III).

TABLE II.—ORIGINAL AND REVIEW PATHOLOGICAL DIAGNOSIS IN ALL CASES

Original pathological diagnosis	Review diagnosis						Total	
	Hodgkin's disease	Other lymph./hæm. system dis.	Malignant, other	Non-malignant	Reviewed, no diagnosis	Not reviewed	Number	Per cent
Hodgkin's disease	422	65	12	12	36	183	730	76.1
Other lymphatic or hæmatopoietic system disease	5	9	1	—	1	11	27†	2.8
Malignant neoplasms, other system	—	—	2	—	—	4	6§	0.6
Non-malignant	1	3	—	11	3	12	30	3.1
Biopsy, no diagnosis	2	2	—	—	4	18	26	2.7
No pathology done	—	—	—	—	—	141	141	14.7
Total	430	79*	15†	23	44	369	960	100.0
Per cent.	44.8	8.2	1.6	2.4	4.6	38.4	100.0	—

*Malignant lymphoma (38), reticulum cell sarcoma (14), giant follicular lymphoma (10), lymphosarcoma (5), mycosis fungoides (5), lymphoblastoma (3), lympho-reticulosis (2), leukæmia (1), and sarcoma (1).

†Bronchus (1), rodent ulcer (1), malignant melanoma (1), connective tissue (1), thyroid (1), prostate (1), testis (2), unspecified or secondary from unknown primary (6), and lymphoepithelioma (1).

‡Lymphoblastoma (18), lymphosarcoma (5), giant follicular lymphoma (2), reticulum cell sarcoma (1), sarcoma, unspecified (1).

§Bronchus carcinoma (2), secondary, primary unknown (1), other and unspecified site (3).

SYMPTOMS

A lump or swelling was the first symptom observed in approximately 60% of those cases for which symptoms were recorded. Constitutional symptoms were recorded in 15% of cases. Pain and other symptoms accounted for the remainder.

The duration of symptoms shows wide variation. Over one-quarter of the patients reported symptoms of two months' duration or less. Of possibly greater interest, about 10% had symptoms two years or longer before reporting for treatment.

METHOD OF TREATMENT

Of the 417 reconfirmed cases (recurrent cases excluded), 326 or 78.2% were treated by radiotherapy alone; in 59 cases chemotherapy was used with radiotherapy; in 21 cases surgery was employed with radiotherapy; four cases were treated by surgery alone and one case was treated by chemotherapy alone.

FOLLOW-UP AND TREATMENT RESULTS

Two kinds of survival rates are presented—crude and adjusted.

(a) The crude survival rate is the number of persons known to be alive at the end of the period considered, divided by the total number who were alive, treated or registered at the beginning of this period.

(b) The adjusted survival rate is the crude survival rate divided by the probability of not dying within a comparable period from any cause other than cancer of the site in question, in a population of the same age and sex composition as the patients comprising the group.

Rates have been computed as at the anniversary of beginning of treatment at the clinics (for untreated cases, at the anniversary of registration). Death registrations were searched in Ontario and a few in Quebec for all cases lost to follow-up at the clinics, and although no death registration could be found for these patients they were assumed for statistical purposes to be dead.

The crude five-year survival rate for all 960 cases with a clinical diagnosis of Hodgkin's disease was 29.7%. For the 730 cases microscopically confirmed, the five-year survival rate was 30.1%. For the 422 cases microscopically reconfirmed the five-year survival rate was 30.3%. The adjusted survival rates were 31.7, 32.1 and 32.2% respectively, or about 7% higher than the crude rates.

The survival rates, both crude and adjusted, for cases reconfirmed as Hodgkin's disease were highest at ages 25 to 34 years (45.3 and 45.8) and substantially higher at ages under 35 than at ages 35 and over. The crude five-year survival rate for males was 27.6% and for females 33.1%.

SURVIVAL BY STAGE

The survival rates on the anniversary of treatment, by single years, for each of the four agreed clinical categories or stages are illustrated in Fig. 1. The excellent correlation between stage and survival is apparent and indicates that this suggested classification of cases by extent of disease is satisfactory for clinical purposes. There is little or no consistent relationship between duration of symptoms and stage of disease, or between duration of symptoms and survival rate.

Hodgkin's disease is similar to cancer in that there are acute and chronic forms of the disease.

TABLE III.—AGE DISTRIBUTION IN MICROSCOPICALLY RECONFIRMED CASES, BY SEX

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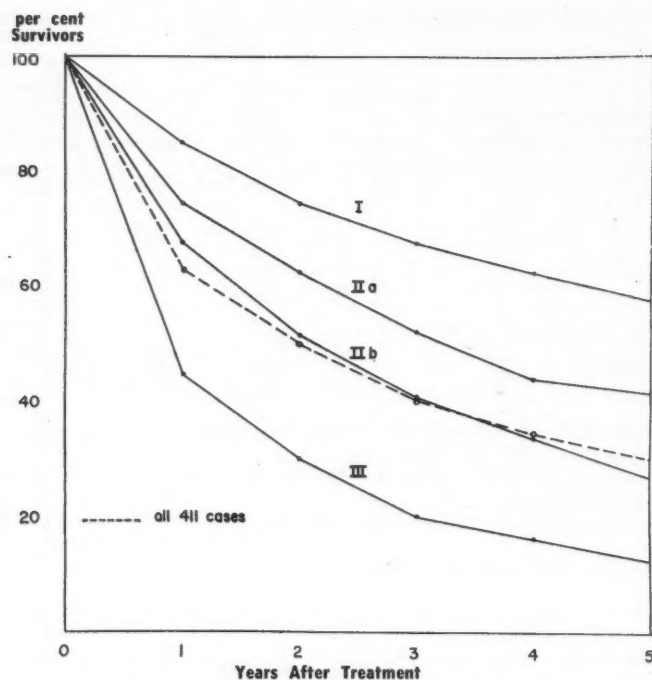


Fig. 1.—Crude survival rates by clinical category—411 reconfirmed treated cases.

The more acute cases usually have diffuse involvement from the beginning with early generalized symptoms and usually do not do well whatever form of treatment is given. The chronic form, on the other hand, may smoulder for years without seriously handicapping the patient's way of life. In the very acute case with symptoms and signs of generalized disease, one is justified in giving a grave prognosis. In any other individual case, it is wise to withhold an opinion concerning prognosis until the response to initial treatment has been observed and until one can get some idea, over the ensuing months, of how the patient and his disease are getting along with one another.

LONG-TERM SURVIVAL

Hodgkin's disease is described as a fatal disease and usually it is. However, most clinics have cases of long survival and some of these are long enough to suggest that in a few cases, at least, Hodgkin's disease does not inexorably lead to death.

The Toronto clinic has a sufficient number of cases treated at least 20 years ago to draw some significant conclusions concerning length of survival of patients. Between 1924 and 1934, 20 cases were confirmed histologically at the time of diagnosis and reconfirmed on review of the sections.

Thirteen of these persons survived five years, eight survived 10, six survived 20, and four are still alive. Some within this group received more radiation than would now be accepted as standard treatment and may even have benefited by the enthusiasm of the pioneers in radiotherapy. Only two had radiation complications of any serious consequence. Of persons admitted up to 1946, 19 have already survived more than 10 years and it is quite possible that 15 of these will reach the 20-year mark. It seems fair to say that, whereas one-

third of patients with Hodgkin's disease die within a year of diagnosis, those who survive to the five-year and especially the ten-year mark have an increasingly favourable prognosis.

The following cases were confirmed histologically at time of diagnosis and reconfirmed on review of the original sections.

CASE 1.—M.L., male. This 24-year-old medical student was diagnosed as having Hodgkin's disease in 1934, having developed a group of nodes in the left cervical chain. One of these nodes measuring 4.5 x 2.5 x 2 cm. was removed and showed the typical features of Hodgkin's disease. He received treatment by x-ray in high dosage to the left side of the neck in December 1934 and January 1935.

In March 1935, nodes recurred on the left side of the neck and definite enlargement of axillary nodes was noted on the right side. Treatment was given to these areas and in smaller dosage as a prophylactic measure to the other lymph node bearing areas. On repeated examination there was no evidence of recurrent disease. He carried on an active medical practice in one of the Toronto suburbs and died of coronary thrombosis 22 years after the onset of his disease.

CASE 2.—H.B., male. Early in 1932 this 31-year-old patient noticed swelling in the left axilla which grew to the size of a large egg over a 15-month period. At the time of examination in April 1933 there were, in addition to the above large node, several smaller nodes in the left axilla. Half of the larger node was removed and reported as Hodgkin's disease. The area was treated by radiation, with disappearance of nodes. In 1935 nodes appeared in the right axilla and recurred in the left axilla. These were treated by x-ray. In 1938 supraclavicular nodes on the left appeared and were treated. In 1944 he developed anaemia and received x-ray treatment for a large mass of nodes occupying the central portion of the abdomen. Further treatment was required to control nodes in the right axilla in 1946 and in 1947. In 1950 widening of the mediastinum and enlargement of nodes in the left hilar region were noted. The patient felt well, however, and no treatment to these areas was given until 1952 when he lost 20 lb. in weight and the masses were noted to have become larger. Following treatment, chest radiograph was reported within normal limits. He remains in good health 26 years after clinical onset of disease.

CASE 3.—D.D., male. This three-year-old boy developed a lump on the left side of his neck in 1932. This gradually increased in size until it filled the whole submaxillary region. A biopsy was performed in January 1934 and the diagnosis was reported as Hodgkin's disease. He received therapy to the neck in January and again in June 1934, followed by a radium pack to the left side of neck in August 1934. In September and November 1935, further treatment to the left side of neck was required. Since then no treatment has been given. He is now 29 and leading a normal life.

CASE 4.—J.G., male. In January 1934, at the age of four it was first noticed that the left side of this patient's neck was swelling gradually. Tonsils and adenoids were removed, with no improvement. Both sides of the neck eventually became involved, the largest node being the size of a lemon. In November

1934, all the nodes were excised from the left side of neck. These were initially reported as paraganuloma. In January 1935 masses recurred along the line of incision. Treatment was given to the neck and axillary areas and later to the mediastinum and groins. In 1939 further treatment was necessary for recurrence of nodes on the left side of the neck. In 1949 he developed pain in the distribution of the lumbo-sacral plexus on the right side accompanied by diminished reflexes. A mass was palpable rectally against the right pelvic wall. Further therapy was given. The patient was last seen in our clinic in September 1955, when he was admitted for asthma. He now resides in Arizona.

CASE 6.—E.L., female. This 19-year-old patient was pregnant when she noticed marked swelling of nodes in both supraclavicular areas, especially the left. Nodes had also become palpable in both axillae. Biopsy revealed Hodgkin's disease. Upon normal termination of pregnancy she received radiation to the right and left supraclavicular areas, the axillae, groins, mediastinum and spleen. This was in 1931. Apart from the development and excision of skin cancer in 1956, in one of the treated areas, this patient has remained well, without evidence of recurrence of Hodgkin's disease.

SUMMARY

The etiology of Hodgkin's disease and some features of clinical interest are briefly reviewed.

Approximately 80 deaths per year in Ontario are assigned to Hodgkin's disease. This is just over 1% of all cancer deaths and about two out of every one thousand deaths from all causes.

The experience with Hodgkin's disease of the eight regional cancer treatment clinics of Ontario from 1932 to 1951 inclusive is reviewed.

During the above period 960 cases were diagnosed clinically as having Hodgkin's disease. Of these, 730 or 76.1% were confirmed on histological examination.

Review by one pathologist of 547 tissue sections previously diagnosed as Hodgkin's disease reconfirmed a diagnosis of Hodgkin's disease in 422.

About four out of five patients were treated by radiotherapy alone. Radiotherapy with chemotherapy, surgery with radiotherapy, surgery alone and chemotherapy alone made up the other forms of treatment, in that order.

There was no significant difference in the five-year survival rates for those patients diagnosed clinically as Hodgkin's disease, those with a diagnosis confirmed histologically, and those reconfirmed as having Hodgkin's disease (crude survival rate—30%, adjusted survival rate—32%).

Hodgkin's disease is not always fatal, as illustrated by the case histories of long-term survivors.

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RÉSUMÉ

Il est juste d'affirmer que peu de progrès a été accompli dans notre connaissance de la nature et de la cause de la lymphogranulomatose maligne depuis la description princeps qu'en donna Hodgkin en 1832. Les auteurs offrent un rappel historique des théories avancées sur l'étiologie de cette affection et le rôle qu'on a attribué à la tuberculose et à la brucellose.

Les recherches dans ce domaine sont rendues particulièrement difficiles par l'absence chez les animaux de lymphogranulomatose spontanée ou transmise, comparable à la maladie humaine. L'anémie que l'on observe dans la majorité des cas est d'origine multiple: hémolyse, myélomatose ou mauvaise utilisation du fer. La ponction de la moëlle prend de l'importance comme élément diagnostique; on conseille de la pratiquer aux endroits de sensibilité osseuse. Il faut se garder, à l'examen des frottis, de confondre mégacaryocytes et cellules de Reed-Sternberg.

Il existe deux écoles de radiothérapie à l'égard de la maladie de Hodgkin: les adeptes de la première croient en l'effet thérapeutique des rayons-x et prétendent prolonger la survie; les membres de l'autre sont convaincus de l'irréductibilité de la maladie et ne se servent de la radiothérapie que pour pallier les symptômes les plus gênants.

Les moutardes azotées sont maintenant acceptées dans le traitement de la maladie de Hodgkin, mais elles ne doivent être employées que dans les formes généralisées ou dans les cas où la radiothérapie a épuisé ses ressources. Les auteurs signalent le Leukeran, de synthèse récente, qui semble offrir certaines promesses dans ce domaine.

L'analyse d'une série de 42 enfants vus au Sick Children's Hospital de Toronto a montré que sauf pour l'absence de localisation digestive, nerveuse ou cutanée, la maladie chez eux n'est pas différente.

La lymphogranulomatose n'est couramment responsable que de 1.14% des morts de cancer et de 0.2% de la mortalité générale en Ontario. De 1932 à 1951, inclusivement, on a compté dans cette province 960 cas de Hodgkin diagnostiqués cliniquement dont 730 (76.1%) furent confirmés à l'examen des tissus. Quatre malades sur cinq requèrent de la radiothérapie; les autres formes de traitement, d'après la fréquence de leur emploi, furent: radiothérapie avec chimiothérapie, chirurgie avec radiothérapie, chirurgie seule et chimiothérapie seule. On n'observa aucune différence statistique significative dans la survie des cas diagnostiqués cliniquement et ceux dont le diagnostic fut confirmé ou même reconfirmé par l'anatomo-pathologie.

Une lueur d'espoir nous est offerte par la relation de cinq cas chez qui la présence d'un Hodgkin fut cliniquement établie et bien confirmée, et où la survie s'étendit au-delà de 20 ans.

INFLUENCE OF STEROID THERAPY ON THE NEPHROTIC SYNDROME IN CHILDREN*

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THE NEPHROTIC SYNDROME in children is, in most instances, a disease entity of unknown etiology characterized by œdema, proteinuria, hypoproteinaemia and hyperlipaemia. At times some degree of hypertension, azotæmia and hæmaturia may occur but this is usually of short duration except in those children in whom the disease progresses to renal failure and death.¹

Although the cause has not yet been discovered, much of the accumulated evidence to date points to an antigen-antibody reaction involving chiefly the basement membrane of the renal glomerulus.^{2, 3} The fact that treatment with steroid hormones will bring about a remission of the disease in 75% or more of children is consistent with this theory.⁴ There is, as yet, no explanation for the failure of the remaining 25% to respond favourably to steroid therapy.

In the past the two major causes of death in this condition were infection and uræmia. With the advent of sulfonamides and antibiotics, it was possible to reduce the mortality due to infection but it seemed that this merely allowed the disease to progress in a greater number of children, thus increasing the percentage mortality from uræmia.

The next important advance in the treatment of the nephrotic syndrome was in 1950 when steroid hormones were first used. In a paper discussing the experience in The Hospital for Sick Children in treating 88 children with steroid hormones between 1950 and 1954, it was pointed out that although 74% of nephrotic children had an excellent response to a course of steroid hormone, recurrence was common weeks to months later.⁴ In an effort to prevent exacerbations, hormone was then given intermittently after the initial course, and our experience since then has shown that in many children this gives a considerable degree of control over the disease.

The natural history of the nephrotic syndrome is one of remissions and exacerbations over a period of one to three years, approximately 50% ultimately becoming cured. The term "cured" must always be used with some reservation, as we have seen at least two children in whom the disease has recurred after a complete remission of over four years. For this reason, it appeared that it would be some years before we could tell whether or not the use of steroid hormones was actually increasing the number of children recovering from

the disease. However, in 1956 Riley⁵ presented a statistical analysis of survival rates in nephrotic children as calculated by a modified life table method. He compared a group of nephrotic children treated before steroid therapy was available with a group treated with these hormones. He has enlarged the size of the group through the co-operation of physicians in other centres. The present paper is a report on the patients treated in The Hospital for Sick Children, Toronto, which forms part of Dr. Riley's survey.

METHOD OF STUDY

The statistical estimation of the survival rate was made on all children with the nephrotic syndrome in whom œdema was initially observed between January 1, 1951, and December 30, 1956. In all, 150 patients with the nephrotic syndrome were seen in the six-year period under study. Only 134 cases could be included in the analysis because of the rigid criteria used for selection: (1) only cases of nephrotic syndrome of undetermined etiology; (2) only patients seen within six months of the onset of œdema.

The method of analysis used was that applied by Riley as outlined by Merrell and Shulman.⁶ Based on a modified life table method, it permits a statistical evaluation of the prognosis of patients suffering from a chronic disease to be made after a short period of observation. Since steroid therapy has been used intensively for only the past four or five years, the longest reasonable follow-up period was set at 48 months. Since new patients appear and others die or are lost from observation at variable times, it is apparent that all patients were not followed up for the 48 months; in fact, of the 134 patients in the study, only 23 were followed up for the full period.

RESULTS

In children with the nephrotic syndrome observed during the pre-steroid period (1946-50), a 61% survival was noted after four years of illness. These results were obtained by Riley⁵ in children seen by him in New York and were influenced favourably by the availability of antibiotics to treat infections, thus providing a slightly improved prognosis from pre-antibiotic estimations of 50% survival.

As illustrated in Fig. 1, the overall survival rate during the study period 1951 to 1956, regardless of method of treatment, was 63% at 48 months. This includes patients receiving no steroid treatment, and sporadic as well as intensive steroid therapy. However, in those children who received an intensive course of steroid therapy, such as that outlined below, the survival rate was calculated to be 81% at 48 months. This figure compares favourably with Riley's of 75% survival, which is the result of the survey including many centres.⁷

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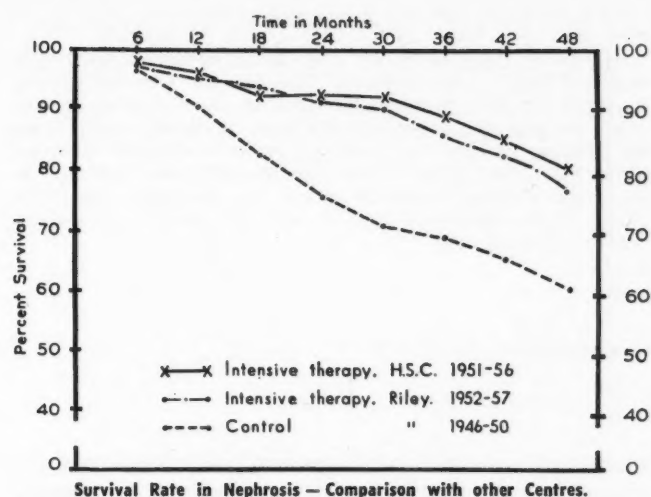


Fig. 1.—The influence of steroid therapy is apparent from 20% improvement in survival rate. The control group in this chart were observed during a period when antibiotic therapy was available; thus the figures for this group do not indicate the more gloomy picture prevailing prior to antibiotic therapy.

The clinical results observed at the 48-month period are shown in Table I. Of the 23 patients followed up for 48 months, 14 are well and give normal results to laboratory tests, five children

TABLE I.—STATUS OF 23 PATIENTS AT 48 MONTHS

Completely well with normal laboratory tests.....	14
Clinically well, persistent proteinuria.....	5
Comfortable but still on treatment.....	1
Refractory to treatment (irreversible renal damage?)....	3

continue to have proteinuria but no oedema, while the remaining four have not responded to treatment. Thus 19 of the 23 patients are living a reasonably normal life four years after the onset of the illness.

PLAN OF TREATMENT

The plan of therapy is similar to that outlined in the previous report from this hospital² and may be briefly summarized:

1. General

1. Bed rest is advisable at the onset and during the oedematous phase. After diuresis occurs, moderately restricted activity is allowed.

2. Foci of infection should be removed and exposure to even minimal infection avoided.

3. Antibiotics in prophylactic doses may be used when infection is present in the home and during exacerbations of oedema until diuresis occurs. The child should receive full therapeutic doses for even minimal infections.

4. Diet consists in restriction of salt during the oedematous phase. However, as much protein as desired is fed. Potassium chloride is given in doses of 1-2 g./day to patients receiving cortisone.

5. No immunization procedure such as DPT or polio vaccination should be undertaken since it is likely to produce a relapse of the disease, possibly

on the basis of an immunological reaction in the body.

II. Specific Treatment

ACTH, cortisone, and the newer cortisone derivatives have all been tried and appear to be equally effective. The dosage of cortisone is approximately 5 mg. per lb. per day given in divided doses. Prednisone is given in one-quarter to one-fifth of this dosage. Injectable ACTH in doses of 20 to 40 units may also be used. Any one of these three preparations may be used when treating a new case. Therapy is continued through the phase of diuresis and until the urine has been free of protein for four to seven days. This usually requires two to four weeks of therapy. If no diuresis occurs after about three weeks, the dose of cortisone (or its equivalents) may be increased to 400 mg. per day for a period of one or two weeks. If there is still no diuresis, the hormone is withdrawn abruptly and this sometimes induces diuresis.

Contraindications to steroid therapy are persistent hypertension, infection, and evidence of progressive renal failure. During steroid therapy, antibiotics in prophylactic dosage should be given, and frequent observations of blood pressure made, since hypertension has been noted not only with ACTH and cortisone but also with the newer, more potent steroids.

After the initial course of treatment, the patient is discharged to continue on intermittent steroid therapy at home. Full therapeutic doses are given three consecutive days each week (every Monday, Tuesday and Wednesday) during the next four to six months. The urine should be tested for protein once or twice a week, and if the urine remains protein-free for this period of time, gradual withdrawal of steroid over several months with progressive reduction in dosage is begun. If a relapse occurs—that is, return of proteinuria or reaccumulation of oedema—continuous therapy is resumed at the same dosage that was used with the initial course. After cessation of treatment, urinalysis should be done every few months as well as during and after any infection, for a period of several years.

CONCLUSIONS

The results of this analysis demonstrate that the four-year survival rate in children with the nephrotic syndrome is considerably increased by intensive steroid therapy. It cannot yet be said that a higher percentage of children are ultimately cured of the disease, since relapses have occurred after four years of apparently normal health; many years of continuing observation will be necessary before this can be shown.

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RÉSUMÉ

Il ressort d'une étude de 134 cas de néphrose lipéidique vus à l'Hôpital des Enfants Malades de Toronto qu'une thérapie intensive aux stéroïdes assure une survie de quatre ans à un plus grand nombre d'enfants que toute autre forme de traitement. On ne peut cependant affirmer que les guérisons soient plus nombreuses puisque des rechutes se sont déjà manifestées après quatre ans de santé apparente. Toute étude définitive dans ce sens demandera encore des années d'observation.

THE TREATMENT OF HYPERKALÆMIA BY CARBOXYLIC ACID RESINS IN THE UPPER AND LOWER GASTRO-INTESTINAL TRACT*

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INTRODUCTION

A MARKED INCREASE or decrease in extracellular potassium concentration may cause serious and sometimes fatal disturbance in muscle irritability and myocardial function. Hypokalæmia can be readily corrected by replacement therapy, but the removal of excess extracellular potassium may be a difficult therapeutic problem.

When renal function is adequate, hyperkalæmia is not encountered very frequently. It may be produced by the parenteral administration of fluids containing large amounts of potassium, particularly in children, or by the rapid release of potassium from cells as in severe dehydration; but when the kidneys are normal, elimination of the excess potassium follows correction of the underlying cause. Similarly, the hyperkalæmia of acute adrenal cortical insufficiency will respond to hormonal replacement therapy.

When renal function is inadequate and unable to respond to corrective therapy, excess extracellular potassium must be removed by other methods. In chronic renal failure, hyperkalæmia is usually a terminal event in an irreversible disease, it is seldom severe, and its treatment is largely of academic interest. On the other hand, in acute renal failure, severe hyperkalæmia may occur early in the illness and cause death in patients who might otherwise recover. Treatment of this complication has included the intravenous administration of solutions containing glucose, insulin, calcium, and sodium, as well as intestinal or peritoneal lavage, hæmodialysis and use of cation exchange resins.¹⁻⁷ The effect of intravenous infusions may be uncertain, while peritoneal and

intestinal lavage have major disadvantages in seriously ill patients. Hæmodialysis promptly controls the serum potassium concentration, and is the only reliable method for use in an emergency; however, it is available only in certain centres and requires the services of experienced personnel.

It is the purpose of this paper to review a three-year experience in the treatment of hyperkalæmia, using carboxylic acid resins* in the upper and lower gastro-intestinal tract. The successful use of resins in three cases was referred to in a previous paper.¹⁰

METHODS

In this study, the sodium and hydrogen cycles of the carboxylic acid resins were used in 13 cases of acute and 4 cases of chronic renal failure complicated by hyperkalæmia. Usually they were mixed in proportions of 7 hydrogen cycle to 3 sodium cycle for use in the upper gastro-intestinal tract, and in equal proportions when used as retention enemata. The proportions were changed if acidosis or elevation of the serum sodium level occurred. In the former case the proportion of hydrogen cycle was reduced and in the latter it was increased.

The resins were administered in the following ways:

1. *Orally*: Ten grams of resin mixture in approximately two ounces of cooked cereal.

2. *By F16 polyethylene intragastric tube*: Ten grams of resin mixture suspended in 70 ml. of water. The tube was flushed with 10 ml. of water both before and after administration to remove gastric contents and residual resins, which otherwise may form a hard paste. Tubing smaller than F16 was found to be unsuitable.

3. *Rectally*: Twenty-five grams of resin mixture suspended in 200 ml. of warm water as a high enema, which was retained as long as possible. Rectal impaction was controlled by a cleansing enema every second or third day.

The resins were administered at intervals of 4 to 12 hours, the frequency being determined by the severity of the potassium toxicity.

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*Provided by Eli Lilly and Company (Canada) Limited, Toronto 13, Ontario.

TABLE I.—THE EFFECT ON SERUM POTASSIUM OF ADMINISTRATION OF CARBOXYLIC ACID RESINS IN RENAL FAILURE

No.	Patient	Cause of renal shut-down	No. of days of resin therapy	Dose of resin in g./day		Pre-resin therapy				Resin therapy			
				Mean	Range	Mean daily output in ml.			Serum K at start of resin mEq./l.	Serum K at end of resin mEq./l.	Mean daily output in ml.		
						Urine	Gastric suction or vomitus	Total			Urine	Gastric suction or vomitus	Total
1. Patients receiving resins orally													
1	N.H.	C ₂ H ₅ OH	3.0	30	11-35	230	0	230	5.6	4.4	488	91	579
2	A.M.	Sub-acute nephritis	9.0	35	10-60	6	0	6	7.0	4.5	4	105	109
3	E.M.*	Septic abortion	7.0	37	10-50	22	36	58	6.0	4.3	390	186	576
4	A.G.	Sub-acute nephritis	4.0	37	15-50	419	71	490	5.2	3.9	70	25	95
5	J.C.†	Shock	2.0	40	20-60	?	?	?	5.7	5.8	730	0	730
6	J.U.	Transfusion reaction	2.0	45	35-55	25	285	310	6.5	6.1	54	0	54
7	K.G.	Afibrinogenæmia	3.0	47	20-50	24	0	24	5.8	5.3	126	33	159
8	E.A.*	Crush	4.0	50	-	12	610	622	6.1	4.2	0	120	120
9	E.W.	Afibrinogenæmia	3.0	50	30-60	129	12	141	5.7	5.0	373	0	373
10	P.G.*	Abortion with hæmolysis	2.0	55	50-60	465	5	470	5.2	3.3	887	75	962
		Mean	3.9	43					5.9	4.7			
2. Patients receiving resins rectally													
11	E.S.	Shock	3.0	66	25-125	150	24	174	6.0	4.0	254	123	377
			2.0	37	25-50	222	0	222	5.3	4.6	335	0	335
			2.0	50	25-75	832	200+	1032+	5.8	4.4	975	0	975
12	E.L.*	Carcinoma ovary with bilat. ureteric obstrn.	4.0	42	24-72	550	0	550	7.6	3.8	217	0	217
13	W.A.	Alcohol, pancreatitis	1.0	50	-	12	610	622	6.1	4.2	0	120	120
14	F.L.	Nephritis	5.0	62	48-72	530	0	530	6.2	3.9	567	0	567
15	J.O.	Shock	4.0	66	24-120	?	?	?	5.7	3.1	122	131	253
16	A.P.	Shock	1.0	100	—	250	0	250	7.6	6.0	485	0	485
17	I.B.	Shock	1.0	100	—	175	0	175	6.1	4.1	165	0	165
		Mean	2.5	64					6.3	4.2			

*Dialysed because of hyperkalæmia prior to starting resin therapy. In all cases there was a rapid rise in serum K in the period (up to 12 hours) between completing dialysis and starting resins. †Thirty-six hours after stopping resins serum K rose to 7.4 mEq./l.

Serum and urinary potassium levels were determined by flame photometry.

RESULTS

Results are summarized in Table I. The table is divided into two sections, the first for resins in the upper gastro-intestinal tract and the second for resins introduced by enema. The cases are arranged in ascending order of administered dose, except for Case 11, in which the resins were administered on three separate occasions. Vomitus and gastric suction are included in the total output, as they were appreciable in some cases and may contain up to 22 mEq./litre.⁸ The output is expressed as a mean of the figures for days prior to starting therapy and a mean of figures for days during the administration of resins. This obscures the occurrence of a starting diuresis but this occurred only in Cases 5 and 10. Case 5 developed severe hyperkalæmia after cessation of therapy, suggesting that the diuresis was not important in the control of his high serum potassium. Cases 5 and 15 were admitted as emergencies without output data some days after the onset of oliguria.

Figs. 1 to 4 show the detailed findings in Cases 11, 12, 14 and 15, given resins by retention enema. All four cases were showing early evidence, on the electrocardiogram, of myocardial toxicity from an elevated serum potassium.

Several features appear from Table I. In the first place it is easier to give larger doses of resin

by enema than it is by mouth. As a result, not only was the duration of administration reduced in the former cases, but also the fall in the serum potassium level was more marked. The mean rate of fall in the oral group was 0.3 mEq./day and in the rectal group 0.8 mEq./day (Table II). At the same time there was a slight increase in vomiting in those patients given the resins by mouth.

TABLE II.—COMPARISON OF ORAL AND RECTAL ROUTES OF ADMINISTRATION

	Route of administration	
	Oral	Rectal
Mean No. of days of therapy	3.9	2.5
Mean daily dose in g.	43.0	64.0
Mean of serum K at start of therapy mEq./l.	5.9	6.3
Mean of serum K at end of therapy mEq./l.	4.7	4.2
Mean rate of fall of serum K mEq./day	0.3	0.8

There are two reasons for the increased dosage by enema. In the first place, patients who received the resins rectally were seen later in the study. With experience the dose was increased earlier in treatment. In the second place, larger tubes can be used for administration by enema, which facilitates the use of larger quantities. Gastric irritability, may also be a limiting factor in oral administration.

Table I shows that no failures were encountered in the control of the serum potassium level after the institution of resin therapy. None of the patients

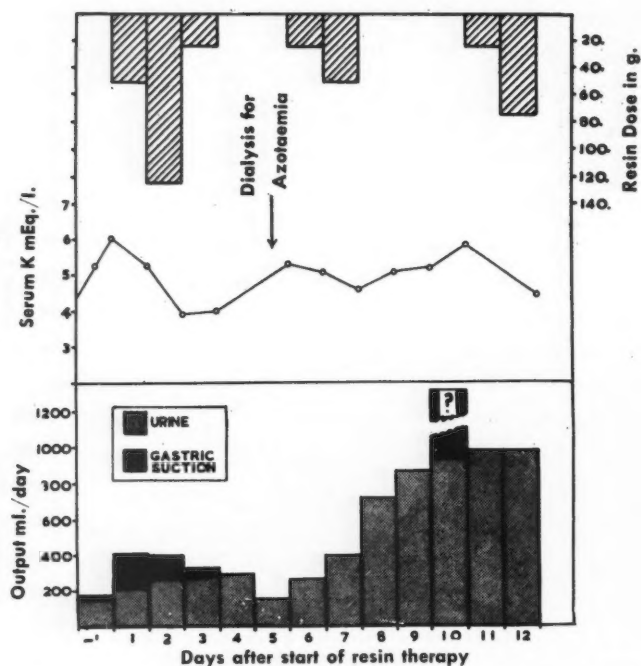


Fig. 1.—Case 11—a 63-year-old male with ischaemic nephrosis.

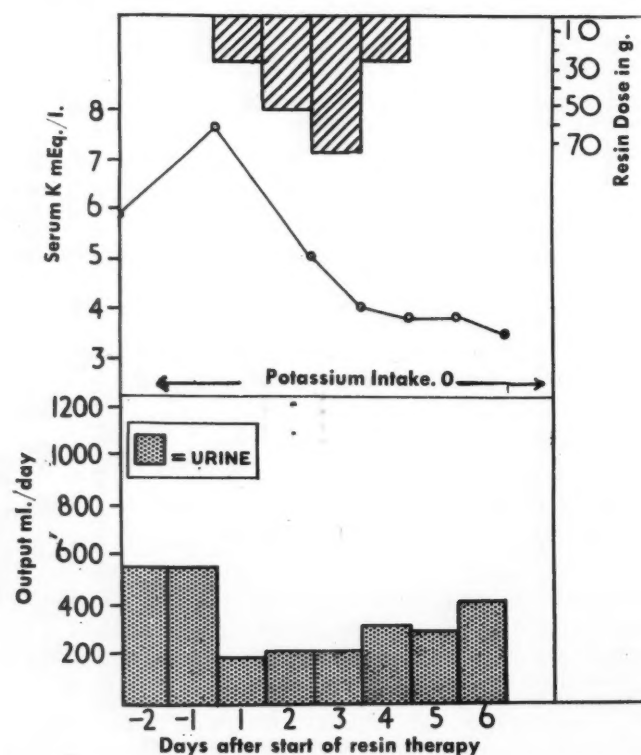


Fig. 2.—Case 12—a 42-year-old female with bilateral ureteric obstruction.

presented here received dialysis for hyperkalaemia, except in Case 5 mentioned above, in which the resins were discontinued because of the impression that they were ineffective.

DISCUSSION

The principle of ion exchange has been used by soil chemists for over a century, and in water softening for nearly 50 years. Synthetic resins which could remove cations or anions from solution

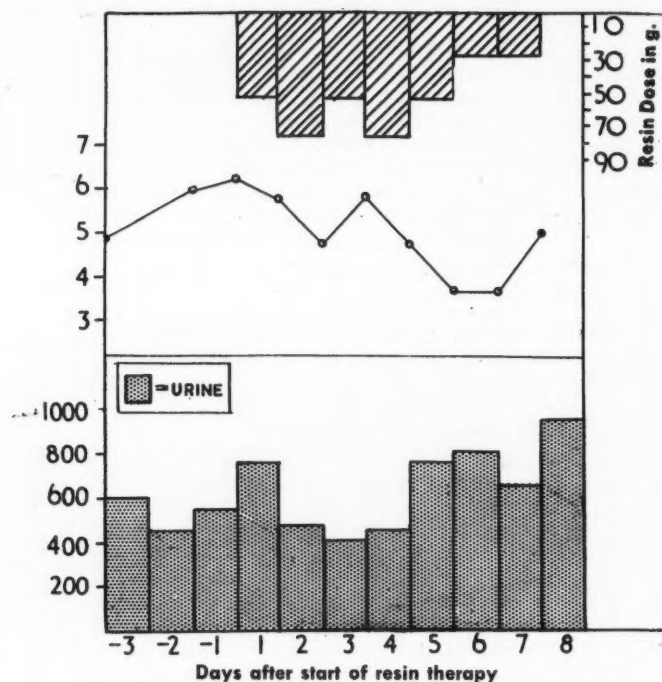


Fig. 3.—Case 14—a 24-year-old male with subacute nephritis.

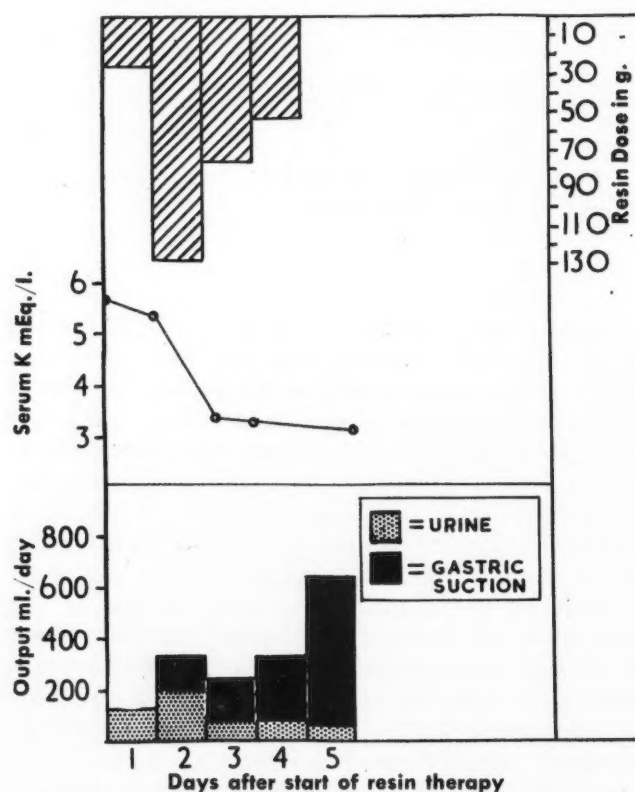


Fig. 4.—Case 15—a 15-year-old male with ischaemic nephrosis.

first became available in 1935, and were widely used in industry and later in biochemical studies. The first clinical application came in 1946 when anion exchange resins were employed to control gastric acidity in patients with peptic ulcer. Shortly thereafter cation exchange resins were employed to remove sodium and potassium from gastrointestinal secretions in clinical disorders associated with retention of these cations.

In 1950 Elkinton and his co-workers¹ first reported the successful use of carboxylic acid resins* in the treatment of anuric hyperkalæmia, and since then several other reports have been published.²⁻⁷

Our observations indicate that all cases of hyperkalæmia will respond to resin therapy if sufficient time is available. A reduction in serum potassium level can be expected within 24 hours, and usually normal values can be restored within 72 hours. In the oliguric phase of acute renal failure, resin therapy should be commenced whenever the serum potassium level is above normal and rising, particularly if there is electrocardiographic evidence of potassium intoxication. Knowles and Kaplan⁴ wait until the serum potassium has reached 6 mEq./litre, but in our experience this may be too late. Case 10 described previously⁹ suffered serious cardiac toxicity, including periods of ventricular arrest when the serum potassium rose from 5.2 to 6.8 mEq./litre within 12 hours.

Hæmodialysis is still the best treatment when there is clinical or electrocardiographic evidence of serious potassium toxicity, as it will reduce the serum potassium level in a few hours. However, for less urgent situations prompt and adequate resin therapy has been so effective that it has rarely been necessary for us to use the artificial kidney for the treatment of hyperkalæmia during the last two years.

The composition and frequency of administration of the resins must be adjusted to the needs of each case, but in all instances therapy should be continued until the serum potassium values are stabilized in the normal range.

Danowski and Mateer⁷ recommended the rectal administration of cation exchange resins for treating hyperkalæmia. However, this recommendation has not been widely followed, presumably because of anticipated difficulties in administration and uncertainty about their efficiency by this route.^{1, 3-5} Observations on man and rats^{11, 12} have shown that there is considerable exchange of potassium across the mucosa of the colon and that it is substantially greater than in other parts of the gastro-intestinal tract. Indeed, the removal of potassium by tap water enemas has been reported in patients with spinal cord disease, one of whom suffered severe potassium depletion.¹³ It is our experience that enemas containing resins produce very little irritation of the bowel and, when given slowly at body temperature, they can be retained even by

seriously ill, disturbed or unconscious patients. At the same time we have found that patients will retain larger amounts of the resin suspension when this is given by retention enema rather than by mouth or intragastric tube. As a result a more rapid reduction of serum potassium level is achieved and the duration of therapy is shortened. Now we rarely administer resins in any other way.

Use of the hydrogen cycle may lead to acidosis due to the exchange of hydrogen for body sodium, especially when compensatory renal mechanisms are inadequate. Similarly the sodium cycle may produce hypernatræmia. Other effects which may occur are electrolyte depletion, faecal impaction due to the insolubility of the resin, and occasionally vomiting or diarrhoea owing to mild irritative qualities of the resin. We have found that acidosis due to the uptake of hydrogen has not been a serious difficulty, as it was anticipated and controlled by appropriate adjustment in the proportion of sodium and hydrogen cycle. We have not encountered calcium depletion, but potassium depletion may occur if the resins are used in the diuretic phase. Hepatic insufficiency is not a contra-indication to resin therapy as long as the ammonium cycle is avoided. In acute renal failure, water balance can be maintained by appropriate reduction in other water intake.

SUMMARY AND CONCLUSIONS

The use of cation exchange resins in the treatment of hyperkalæmia occurring in 13 acute cases and four cases of chronic renal failure has been reported.

Resin therapy is effective, safe and simple in its application. It should be employed in all cases of hyperkalæmia, except those in which life-threatening cardiac toxicity is already present; the latter should be treated by dialysis.

Owing to the active transfer of potassium across the colonic mucosa, the removal of body potassium by retention enemas containing cation exchange resin is highly effective.

The administration of the resin by retention enema is more effective than its administration into the upper gastro-intestinal tract, as it is easier to give larger doses.

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*Carboxylic acid resins are organic macromolecules which contain a carboxylic acid group as an integral part of their structure. This group, either in the free acid form or in the salt form, enables the molecule to exchange cations when it is treated with solutions of various electrolytes. In order to be useful as a cation exchanger the resin must be almost completely insoluble in the electrolyte medium with which it comes into contact. The exchanging ion is commonly either hydrogen, ammonium, sodium or potassium and the resins are said to be in the corresponding "cycle". When introduced into a solution of electrolytes, ionic exchange takes place until the cations are in equilibrium. The various cycles are not selective, but when equivalent concentrations of ions are present the order of preference for exchange of these ions is such that potassium and then sodium are rapidly bound by the resin and so removed from the environment.

POLIOMYELITIS IN WINNIPEG —1958: EPIDEMIOLOGICAL STUDY, INCLUDING THE EVALUATION OF ARTIFICIAL IMMUNIZATION

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In 1953 in the city of Winnipeg, 763 cases of poliomyelitis were reported.¹ The incidence in that epidemic was the second largest that has occurred in North America in an urban population of over 200,000. In the following year, there were 23 cases, in 1955 three cases, and in 1956 and 1957 two cases. In 1958, up to December 1, 76 cases were reported.

vaccine and a 35-year-old non-immunized man. They both developed the disease on the same day. Although they lived in the same district, no evidence of direct contact was established, though the boy was a constant playmate of the man's children. It would appear that both these fatalities resulted from a massive dose of infection from a common source.

EPIDEMIOLOGICAL VARIATION

In 1958, three cases of paralytic poliomyelitis occurred in the first two weeks of June. If these cases had proved indicative of the epidemiological pattern of previous epidemics in Winnipeg, the incidence would have risen each week until the 10th or 12th week, when the epidemic would have reached its peak with the reporting of approxi-

TABLE I.—POLIOMYELITIS IN WINNIPEG—1958, CASES BY AGE AND SEX DISTRIBUTION

Age Group	Total	Per cent of total	Male			Female		
			With paralysis	Without paralysis	Total	With paralysis	Without paralysis	Total
0 - 4.....	28	36.8	13	3	16	10	2	12
5 - 9.....	13	17.1	8	3	11	1	1	2
10 - 14.....	4	5.3	2	1	3	0	1	1
15 - 19.....	2	2.6	0	0	0	1	1	2
20 - 29.....	20	26.3	9	5	14	2	4	6
30 - 39.....	6	7.9	3	1	4	2	0	2
40 and over.....	3	4.0	1	0	1	0	2	2
Total.....	76	100.0	36	13	49	16	11	27

AGE AND SEX DISTRIBUTION

Table I shows the age and sex distribution of the reported cases in the 1958 outbreak:

(a) The highest incidence (36.8%) of the disease occurred in the 0-4 year age group.

(b) The lowest incidence (2.6%) of the disease occurred in the 15-19 year age group. In the 1953 epidemic in Winnipeg, the lowest incidence was also in this age group.

(c) Thirty-eight per cent of the cases were in persons 20 years of age or older.

(d) There was a considerably higher incidence in all age groups in males than in females.

PARALYSIS-MORTALITY

At the time the case was reported, 68.4% of the patients had some degree of paralysis and there was a considerable variation in the percentage of cases with paralysis among the various age groups (Table I); 82.1% of cases in the 0-4 year age group were paralytic.

Four adults—three men and one woman, one five-year-old boy and one infant of five months—died, a mortality rate of 7.9. An indirect contact relationship occurred in two of the fatal cases. The patients involved were a five-year-old boy who had previously received two doses of poliomyelitis

mately six times the number of cases occurring in the first week; the incidence should then have rapidly receded.

In 1958, however, although there was but a tenth of the number of cases that had occurred in the 1953 epidemic, the previous epidemiological pattern of the Winnipeg epidemics was closely followed up to a peak in the 11th week with subsequent recession, but there was a variation from the previous pattern in that during the 13th and 14th weeks the incidence again rose. This delayed peak of incidence occurred during the first and second weeks after the opening of schools (Fig. 1).

No previous epidemics in Winnipeg had shown similar patterns with this delayed peak. In the 13th and 14th weeks of the epidemic, a total of 17 cases occurred. Ten were in adults, four in children attending school, and three in children of pre-school age. Three of the adults and two of the school children became paralyzed. One of the paralyzed school children had entered school for the first time and therefore had not been included in the school immunization program carried out over the last two years. The other paralytic case occurred in a nine-year-old boy whose mother had refused to allow him to be immunized in the school immunization program. Of the three cases in pre-school children, two were paralytic and one was non-paralytic. These 17 cases which occurred after the opening of schools represent a deviation from the epidemiological pattern of previous

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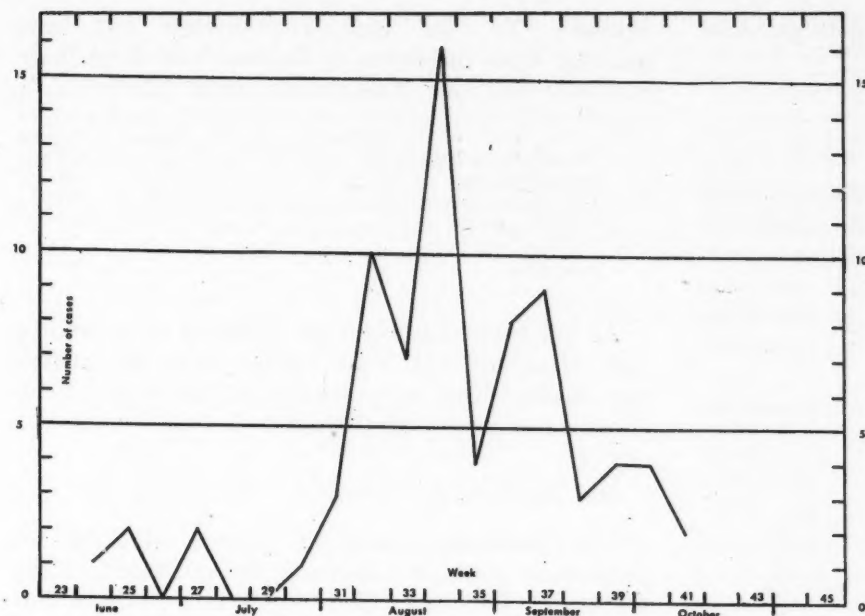


Fig. 1.—Poliomyelitis in Winnipeg: cases reported during 1958.

epidemics of the disease in Winnipeg. The only apparent new known factor in the community was that approximately 100% of the 50,000 school children had been immunized. An increased carrier state among the immunized school children, coincident with the opening of the schools, could have been responsible for an increase in dissemination of the virus and an increase in the incidence among non-immune adults and children of pre-school age.

IMMUNIZATION STATUS OF CASES

Of the 52 patients who became paralyzed, 39 had received no vaccine, 8 had received one dose, 3 had received two doses, and 2 had received three doses (Fig. 2). Type I virus was isolated from the latter two cases.

Of the two paralyzed persons who had received three doses of vaccine, one was a 14-year-old boy who developed only minimal weakness of the deltoid muscle. The spacing of the inoculations which this boy had been given was not as recommended for obtaining maximum immunity, in that only three months had elapsed between the second and third inoculations. The other case was in a four-year-old girl who developed extensive paralysis in both legs. Results of chemical and electrophoretic analysis of this latter patient's plasma proteins were as follows: (chemical) total protein 7.06 g. %; albumin 5.29 g. %; globulin 1.77 g. %; (by electrophoresis) albumin 59.5% (4.2 g. %); alpha 1 globulin 2.28% (0.16 g. %); alpha 2

globulin 14.5% (1.02 g. %); beta globulin 15.26% (1.08 g. %); gamma globulin 8.39% (0.59 g. %). If the range of normal values for the globulin fraction are taken as 10-22%,² this girl's gamma globulin level was less than the lower limit of normality. There had been nothing in the previous history to suggest gamma globulin deficiency, but these findings are of interest in this case.

Of the 24 non-paralyzed patients, 11 had received no vaccine, 3 had received one dose, 2 had received two doses, and 8 had received three doses. Seven of the 8 who had received three doses of vaccine and were reported as having non-paralytic poliomyelitis were admitted to

the King George Isolation Hospital. In only 3 of these cases was poliovirus isolated, and the validity of the clinical diagnosis in the remaining 5 cases could be questionable.

In Winnipeg there are approximately 22,000 children in the age group 2 to 5 years. The personnel of the City Health Department had immunized approximately 9000 of this group, and an estimated additional 9000 had been immunized by private physicians. In the remaining, approximately 4000, non-immunized children of this age period 20 cases occurred. This is a case rate of 500 for 100,000 population in this non-immunized age group. If this case rate had been shown in the balance of the population, it would have been equivalent to 1200 cases, but this did not occur in the balance of the population of approximately 250,000. The fact that the number of adults who had received vaccine was limited would indicate a high level of natural acquired immunity in those who had resided in the city for more than

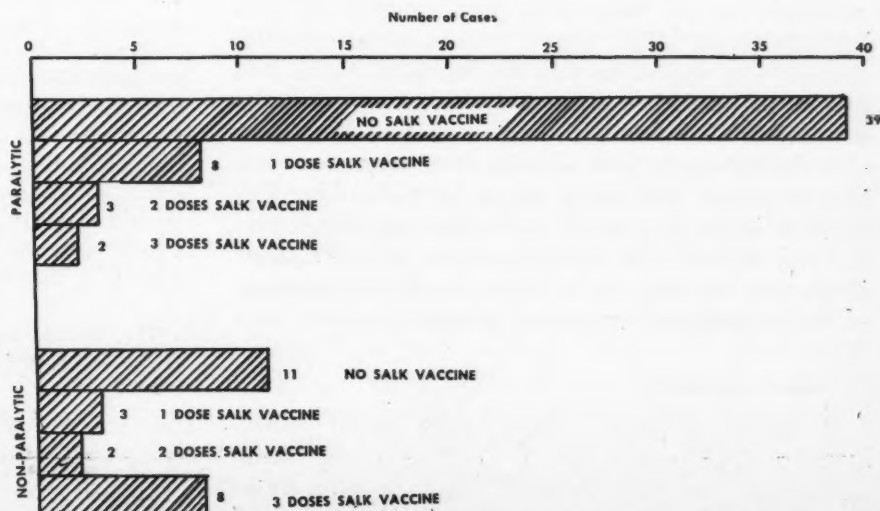


Fig. 2.—Immunization status of paralytic and non-paralytic cases of poliomyelitis in Winnipeg, 1958.

five years and hence had been exposed to previous epidemics.

RELATION OF ONSET OF DISEASE AND IMMUNIZATION

In the last two years over 200,000 doses of polio vaccine have been given in the schools and in the child health centres. This has been further implemented by a full-scale immunization program carried out by private physicians. It is, therefore, reasonable to assume that if such an extensive

TABLE II.—IMMUNIZATION DURING INCUBATION OF POLIOMYELITIS (7 CASES)

Age	Sex	No. of doses	Date of doses	Onset date of disease	Paralytic or non-paralytic
6 years	F	2	April 30/58 May 28/58	June 8/58	Paralytic
6 years	M	1	Sept. 7/58	Sept. 13/58	Paralytic
33 years	M	1	Sept. 8/58	Sept. 17/58	Paralytic
7 mos.	F	1	Aug. 19/58	Aug. 22/58	Paralytic
17 years	F	1	Aug. 7/58	Aug. 10/58	Paralytic
18 years	F	2	July 23/58 Aug. 3/58	Aug. 6/58	Non-paralytic
28 years	M	1	Sept. 18/58	Sept. 24/58	Non-paralytic

immunization program were carried out during the course of an epidemic, some individuals would receive the vaccine while they were actually incubating the disease. The record of the cases in Table II discloses this factor. There is also a sequel in such cases, in that there may be a tendency for some individuals to incriminate the administration of the vaccine as the cause of the attack.

INFLUENCE OF PREVIOUS RESIDENCE IN WINNIPEG

An analysis was made to determine whether previous residence in Winnipeg was a factor in the 1958 epidemic. Excluding those five years old and under who had developed the disease and who had been born since the epidemic of 1953, there was a total of 41 cases. Twenty-seven of these cases were in persons who had lived in Winnipeg since before 1953 and the remaining 14 cases occurred in persons who had moved into Winnipeg since that time. No accurate statistics are available on the number of new immigrants into the city since 1953, but if the incidence of the disease was approximately the same in these two groups, it would represent 120,000 new arrivals; actually it is estimated that there had been less than 20,000 such new arrivals. It is apparent that the incidence was much lower in those who had lived in Winnipeg before 1953 than in those who had moved into Winnipeg since that time. Artificial immunization was not a factor in the comparison of the incidence in these two groups.

VIRUS ISOLATION

Wherever possible, faeces and paired blood samples were sent to Dr. J. C. Wilt in the Virus Laboratory for virus identification. Seventy-three out of the 76 cases were treated in hospital, and virus study was possible in the majority of cases

notified. To date type I poliovirus has been isolated from the faeces in 52 cases and from brain tissue in one case. The results are as follows:³

No. of cases examined	73
No. of results	66
Poliovirus, type I	53
ECHO 6 virus	1
Unidentified virus	1
Negative	11

As yet there has been no isolation of poliovirus type II or type III. Virus studies were not carried out on the three cases treated at home and these three cases were non-paralytic.

USE OF GAMMA GLOBULIN

The protective value of gamma globulin for household contacts had been demonstrated in the 1953 polio epidemic,¹ and largely as a result of this experience it was made available, free of cost, to all household contacts during the 1958 epidemic. The suggested dosage was 5 c.c. for contacts weighing under 35 lb., 10 c.c. for those weighing between 36 and 60 lb., and 15 c.c. for those over 60 lb. These facilities were extensively used. No cases of poliomyelitis developed in the household contacts who had been given gamma globulin. There were three instances where multiple cases of polio developed in the same household, but these families did not receive gamma globulin, for various reasons beyond our control.

SUMMARY

The City of Winnipeg experienced an outbreak of poliomyelitis during the summer months of 1958, and 76 cases were reported. The highest incidence of the disease occurred in the 0-4 year age group, 82.1% of the cases in this group being paralytic. Only two of the 52 paralyzed patients had received three doses of poliomyelitis vaccine, and one of these had not received the third dose of vaccine at the recommended interval of seven months. The statistics indicate that a high degree of protection against type 1 virus was afforded by the use of the recommended immunizing doses of poliomyelitis vaccine. Apparently the use of gamma globulin in household contacts was of definite value. Comparison of the incidence of the disease among recent arrivals to Winnipeg and those who had been residing in Winnipeg before 1953 indicated that there is a relatively high degree of naturally acquired immunity in the latter group. A second rise in incidence of cases, the majority of which were in adults, occurred after the opening of schools in September.

The vaccine used for immunizing residents of the City of Winnipeg was produced by Connaught Medical Research Laboratories.

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RÉSUMÉ

On rapporta 76 cas de poliomyélite au cours de l'épidémie qui sévit à Winnipeg pendant l'été 1958. Les enfants de quatre ans et moins furent les plus fréquemment atteints, (82.1% de ce groupe souffrirent de paralysie). Seulement deux des 52 malades paralysés avaient reçu trois doses de vaccin anti-poliomyélique et l'un d'eux n'avait pas reçu la troisième injection à l'intervalle indiqué de sept mois. Les statistiques montrent que le vaccin aux doses

recommandées, procura une forte immunité contre le virus de type 1. Il semble que la globuline *gamma* ait été utile dans la protection des personnes exposées au contagement dans une même famille. La fréquence de l'infection chez les personnes arrivées à Winnipeg depuis 1953 comparée à celle observée chez les résidents établis dans cette ville depuis plusieurs années, montra que ceux-ci avaient acquis une forte immunité naturelle. Une seconde recrudescence de l'infection, surtout chez les adultes, se produisit après la rentrée des écoles en septembre.

THE SURGICAL MANAGEMENT OF VARICOSE VEINS COMPLICATING PREGNANCY

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DURING THE SUMMER of 1949, our obstetrician became interested in the surgical management of varicose veins complicating pregnancy and requested that one of his pregnant patients be treated by multiple high and low ligation of the long saphenous system in both lower extremities. To our surgical group this seemed like a radical departure, and it was with some trepidation that the procedure was carried out on a patient then 5½ months' pregnant. An extremely satisfactory result was obtained. Since that time we have carried out the procedure on a small series of cases (including the wife of the obstetrician) which we wish to report.

Our present solution to the problem is designed to:

1. Try to permanently relieve the severe distress associated with the second half of pregnancy, necessitating marked curtailment of normal activity during the latter weeks.
2. Eliminate the danger of a blowout.
3. Prevent phlebitis in the post-partum period.
4. Avoid recurrence in subsequent pregnancies.

REVIEW OF THE LITERATURE

Barrow¹ states that "pregnancy is not regarded as a contraindication to this simple operation if the operation is necessary for the patient's welfare." We agree with Shank² that cases for operation must be carefully selected and should include only those patients suffering from types III and IV veins. Shank classifies varicosities as follows:

Type I—"Consists of fine cutaneous dilatations of the stellate design."

Type II—"This is the isolated saccular varix usually appearing along the course of the great saphenous vein."

Type III—"This is the fully developed tortuous cavernous mass of varices, either in the great or small saphenous vein."

Type IV—"This is the varix of uniform dilatation of a large trunk. The walls of these veins are markedly hypertrophied and undergo a dilatation with persistent increase in pressure. This may be seen on all parts of the thigh and lower leg."

Greenstone⁴ considers that "there is no longer any doubt that extensive operation on veins is reasonably safe during pregnancy, but to recommend that it be done routinely for varicosities in pregnant women would seem to disregard the fact that the aggravating factor in bringing about the varicose condition is not removed."

Lobraico⁸ thinks that "varicose veins associated with one or more incompetent veins in pregnancy as well as at other times are best treated surgically. Sclerosing substances are not recommended since they will not work in a high pressure dilated system, and if they do locally obstruct the vessel, the high pressure will merely bring about the development of collateral varicose veins."

Luke⁶ states that it has been his practice to treat varicose veins conservatively in pregnant women, "but if the patient insists on something being done, or if the symptoms are severe, stripping can be performed. In such cases, the superficial external pudendal branch should be followed as far into the labia as possible to eliminate vulvar varices. Patients should be warned that despite a previous stripping operation, a later pregnancy will cause reappearance of varices in formerly uninvolved branch veins. Also, bluish blemishes caused by masses of dilated venules will reappear, but most will subside at the end of the pregnancy or any remaining may be treated by local injections."

Solomons⁷ agrees that the condition should be treated, but prefers to do it conservatively by injection with a sclerosing agent and the wearing of elastic supports. However, he states that it is most unsatisfactory to say that: "(a) treatment is unnecessary because varicosities always get better; (b) treatment is useless because varicosities always recur."

Fegan⁵ considers that "since surgery would not be countenanced during pregnancy a number of women would not receive any treatment". However, he does report a series of 328 pregnant patients treated by injection of Sotradecol, the injections being anywhere from the ankle to the

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labia. Myers and Smith⁹ list pregnancy as one of the contraindications to surgery, but do not amplify this.

PERSONAL SERIES

Since October 1949, we have treated varicose veins surgically in seven pregnant women, operating on a total of eleven involved legs. Between October 1949 and May 1953, we treated three patients, two by bilateral high and low ligations and the third by ligation on the right side only. These patients were admitted to hospital, the operation was performed under local anaesthesia, and the patients were asked to get out of bed the same afternoon. These patients all had satisfactory results. Two of them became pregnant again, one requiring three local vein injections and the other requiring nine injections during the pregnancy. Both these patients remarked on the improvement in, or lack of, symptoms during the subsequent pregnancy.

During May 1953, a patient five months' pregnant was admitted for operation for bilateral incompetence. At this operation one extremity was treated by multiple high and low ligation and the other extremity by multiple high and low ligation plus stripping of the long saphenous vein. Postoperatively the leg in which the vein had been stripped was symptom-free while the other leg continued to produce varices and was painful. A stripping procedure was carried out on this leg at the beginning of a subsequent pregnancy, at the patient's request; during a third pregnancy both lower extremities were symptom-free and she has not required any injections. Since that time we have adopted the procedure of multiple ligation plus stripping wherever possible.

Our patients are carefully selected before operation is suggested. If the procedure is contemplated, we limit our selection to patients with type III and IV veins.² We make certain that the deep system is patent and has not been obliterated by a previous thrombophlebitis. We use the elastic bandage or elastic stocking test, as suggested by Sullivan,³ and are extremely cautious if wearing of a tight support increases the patient's distress. The tourniquet test is also used on all patients.

The patients are admitted to hospital on the afternoon before operation, the veins are marked with vein-marking ink, the extremities are prepared and the patients are given a sedative at bedtime. The operation is performed under general anaesthesia, usually with sodium thiopentone (Pentothal), nitrous oxide and oxygen. Postoperatively, the foot of the bed is elevated one notch for 24 hours and the patients are requested to get out of bed on the first postoperative day. The patients are discharged between the third and seventh postoperative days and the sutures are removed on the seventh day either in hospital or the office. Pressure bandages of the Ace type, which are applied from toes to

groin immediately postoperatively, are worn when the patient is ambulatory, until two weeks post partum. If the above-knee varicosities are not too severe preoperatively, the Ace bandage from knee to groin is removed three weeks postoperatively.

Since 1953, we have treated five legs by multiple ligation and stripping, with what we consider very satisfactory results. We have not had any complications and the patients have been very grateful, because symptoms were relieved and they were better able to live the normal life of a pregnant woman than before operation. It has been our feeling that we prefer to operate before the sixth month of pregnancy.

After termination of pregnancy, the patient is requested to come in for observation every three months; when necessary, injections are carried out in the office with 1 or 3% Sotradecol. Should any of these patients become pregnant, the legs are examined by the surgeon each time the patient comes in for prenatal examination.

Our records show that the procedures were carried out at the following times: one at 3 months; three at 5½ months; one at 6 months; one at 7 months; one at 8½ months.

The last case is of interest because, if we had realized the duration of the pregnancy, we probably would not have advised the operation. In this case the patient claimed to be six months' pregnant, but one month after operation a full-term child was born. This patient almost demanded treatment because of her symptoms; operation on the right leg was completed but, because of excessive bleeding after this procedure, only a token ligation of isolated varices was carried out on the left leg. In keeping with our previous postoperative findings the right leg was satisfactory but the patient continued to complain bitterly of the veins on the left lower leg, which were eventually injected post partum. On looking back, we now feel that we should have completed the surgery on the left leg at the first operation, because the left leg will give trouble with any subsequent pregnancy.

Follow-up of these patients shows that those who had only multiple high and low ligations required subsequent injections post partum; one patient during a subsequent pregnancy had nine injections. None of the patients who had multiple high and low ligations with stripping have required subsequent injections. One patient in this category is again pregnant and at five months complains of an occasional cramp in her foot. She also has a small varix on the medial side of the knee which may require injection.

CONCLUSIONS

From our small series of cases we conclude that:

1. The severe symptoms in the lower extremities occasioned by the combination of pregnancy plus severe varicose veins of Types III and IV can be relieved by operation.

2. The operation of choice is multiple high and low ligation with stripping of the long saphenous vein from ankle to groin, and/or short saphenous when indicated.

3. The procedure does not endanger the pregnancy.

4. The optimum time for operation is before the sixth month.

5. The procedure is justified, as evidenced by the marked relief of symptoms and the apparent lack of complications.

SUMMARY

The literature on the surgical management of varicose veins complicating pregnancy is reviewed. Eleven cases treated surgically since 1949 are reported, together with a description of the procedure, the type of follow-up used, and our conclusions.

ANALYSIS OF INTRAUTERINE MALFORMATIONS OF THE VERTEBRAL COLUMN INDUCED BY OXYGEN DEFICIENCY*

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INTRODUCTION

THE RESULTS of experiments in developmental physiology and biochemistry in the last few years have brought us new information on the origin of malformations in human beings and animals. Experimental studies on amphibian and chick embryos have shown that certain embryonic aberrations of structure can be produced by varying degrees of damage to the metabolism of the anlagen of certain organs. The intensive oxidative processes preceding the formation of the blastema coincide with the sensitive phases of development. These are also periods of susceptibility to any deleterious effects of genes.

In experiments on mammals, however, difficulties have arisen because the environment of the embryo *in utero* cannot be so systematically and deliberately altered as is possible in experiments on amphibian and chick embryos. Our experimental work with rabbits therefore began with the aim of producing similar malformations in embryos at the corresponding stage of development by subjecting them to a single exposure of about four

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RÉSUMÉ

L'inconvénient que comportent les veines variqueuses avancées, pendant la grossesse, peut-être supprimé par la chirurgie. L'intervention de choix consiste à pratiquer la ligature haute et basse avec dénudation de la grande saphène de l'aine à la cheville et aussi de la petite saphène s'il y a lieu. La grossesse n'est exposée à aucun danger et la période la plus propice à cette opération s'étend jusqu'au cinquième mois. L'amélioration qui en résulte ainsi que l'absence de complication justifient l'application de ces mesures.

hours of oxygen deficiency. The successful researches of the teams led by Prof. Buchner in Freiburg, Prof. Ingalls in Boston, Prof. Murakami in Nayoga and Prof. Werthemann in Basel served as models for our own experiments.

PRELIMINARY DATA

We were able to produce disturbances in the early anlage of the vertebral column between the 8th and 10th days of embryonic development in rabbits. Sensitivity to such alteration was greatest on the 9th day of pregnancy. Fig. 1 shows concisely the results we have obtained to the present time. The abscissa reading from left to right indicates increasing intensity of oxygen deficiency in regular stages from 21,000 to 30,000 feet. The ordinate indicates the percentage of malformations of the spine. The lines rising diagonally in the third dimension indicate the progress of pregnancy between the 8th and 10th days after conception. The diagram shows the results of examination, by means of (a) x-ray or (b) staining by alizarin and clearing by benzyl alcohol, of 145 litters containing 671 animals. A clear connection can be seen between the intensity of the oxygen deficiency in the critical days of pregnancy and the degree of spinal deformity, on the one hand, and the effect of sensitivity of the axial metabolic gradients on the extent of these anomalies, on the other hand.

As early as 1955, these results inspired us to investigate, in collaboration with the Anatomical Institute of the University of Cologne, the early embryonic development of the vertebral column under normal and pathological conditions.

We were able to prove at that time, by means of carefully prepared sequences of sections of 11-

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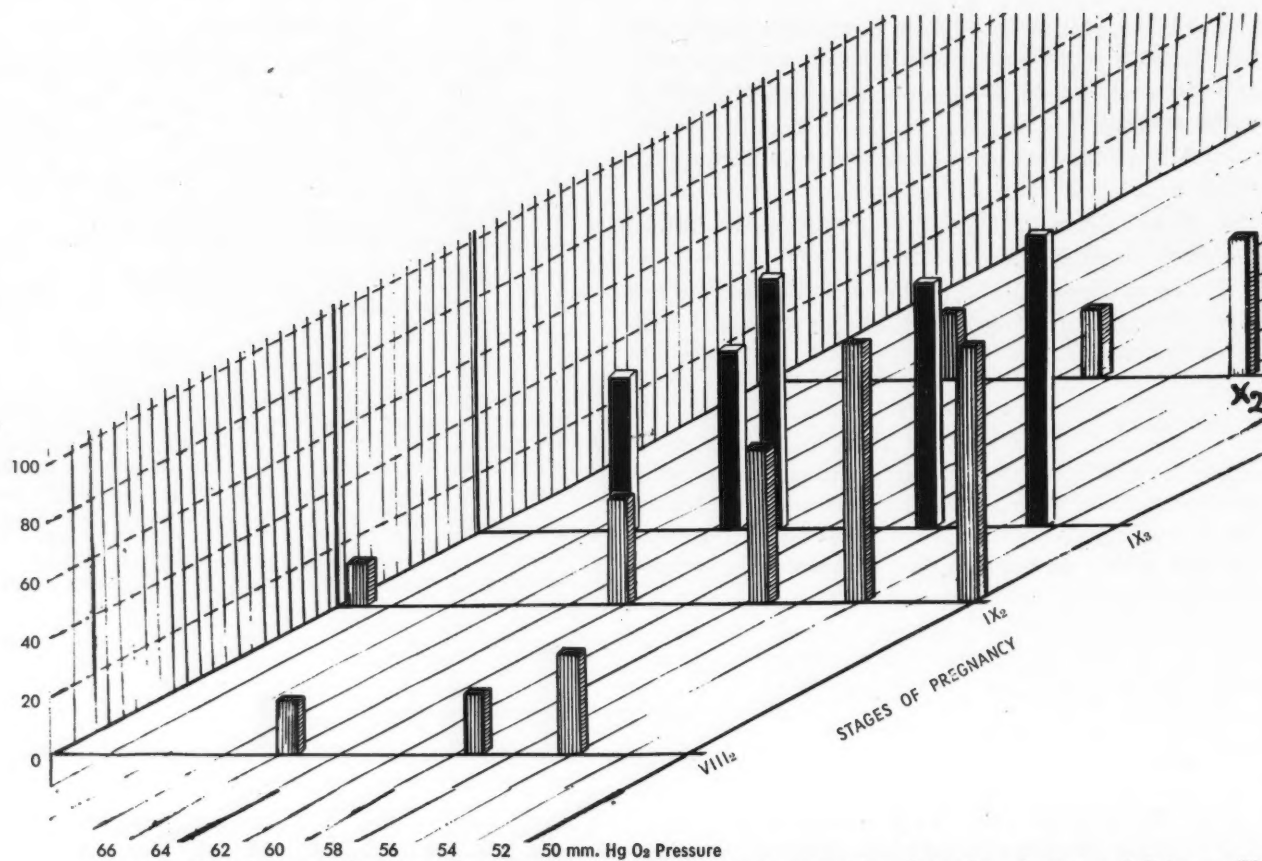


Fig. 1.—The diagram shows at the abscissa from left to right increasing intensity of oxygen deficiency. The ordinate indicates the percentage rate of malformations. The lines diagonally indicate the progressing pregnancy (8th-10th days).

12- and 13-day-old embryos exposed to oxygen deficiency on the 9th day, that it is the notochord which is damaged and not the periaxial blastema. At the height of metabolic activity of the notochord, an induced deficiency of oxygen causes damage to the cytoplasm and nuclei of these cells. This damage to the metabolic function of the cells of the notochord results in changes in tension which alter the statics of the normally taut, elastic notochord in this region. This in turn leads to bending, cracking and tearing of the covering of the notochord. The result is a faulty induction of the adjoining periaxial mesoderm. Histological researches on these embryos have in the meantime been systematically continued in collaboration with Dr. Knoche of the Anatomical Institute of the University of Münster. Our aim has been to obtain a better insight into the normal and pathological intrauterine development of the axial skeleton through careful analysis of the successive stages of embryonic development, first by morphological and later by histochemical methods.

RECENT STUDIES

From a series of rabbit does subjected to extreme oxygen deficiency (about one-third of normal oxygen tension) lasting about four hours on the 9th day of pregnancy, we obtained 112 embryos and fetuses out of 15 pregnancies by interrupting the gestations. The embryos were treated with Bouin solution and in some cases with Zenker

solution, and blocked in paraffin. Frontal and in some cases sagittal sections were made, all stained with Weigert's hæmatoxylin, of 16 embryos at consecutive stages of development, at intervals of two days from the 11th to the 27th day. A control series shows the same stages of development in 12 sections.

The illustrations show some of the anomalies induced in the intrauterine development of the vertebral column after damage by oxygen deficiency.

Fig. 2 shows the stage of development of a nine-day-old rabbit embryo at the time when its mother was subjected to oxygen deficiency. The embryo,

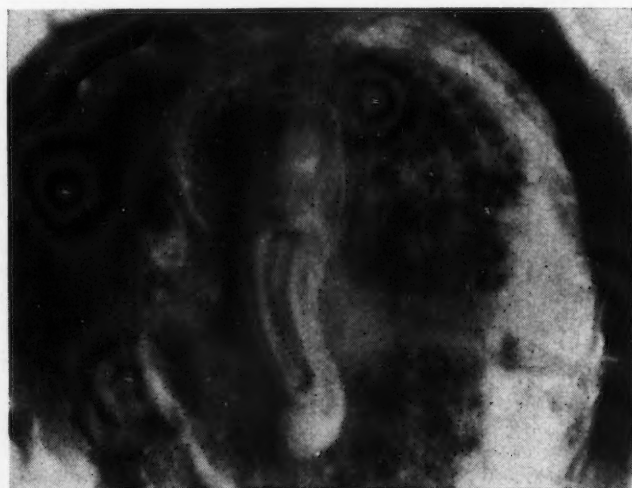


Fig. 2.—Rabbit embryo 9 days old (length: 4 mm.)

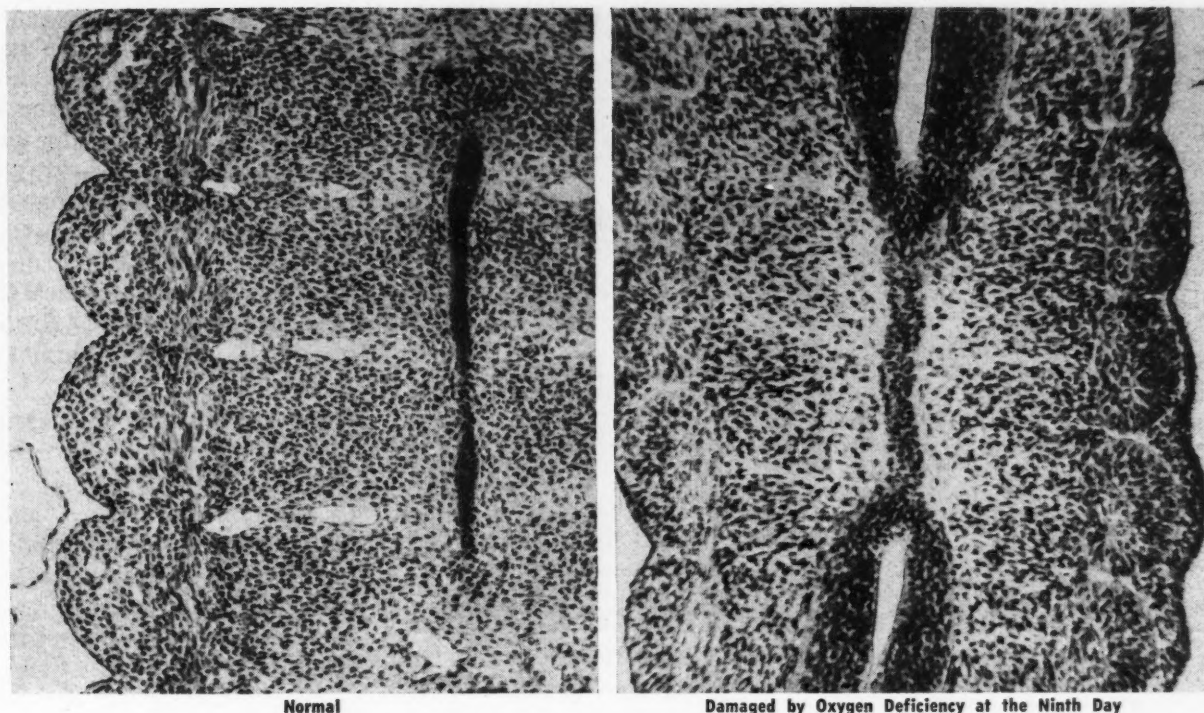


Fig. 3.—Frontal sections of the central part of two 11-day-old embryos.

which is about 4 mm. long, has approximately 15 primitive segments on either side. The notochord has been separated from the entoderm. By this stage the medullary tube is already almost completely closed dorsally.

Frontal sections of the central part of the two 11-day-old embryos are shown in Fig. 3. On the left is a general view of a normal embryo. In the midline the notochord is seen. The periaxial mesoderm is already clearly segmented. The bilaterally symmetrical lighter areas show the position of the intersegmental fissures. The regular, dense covering of the periaxial mesenchyme about the notochord is to be noted. The picture on the right shows, even at this early stage of development, the first effects of damage caused by oxygen deficiency. The notochord plainly bends away from the midline. The periaxial mesenchyme around it is noticeably looser, and in places perichordal gaps can be seen. Here, too, the periaxial mesenchyme already shows segmentation in the form of metameric arrangement of intervertebral fissures, but the close contact between the notochord and the mesenchyme appears to have been greatly disturbed. This hinders the laying down of building material for the vertebral bodies and the intervertebral discs.

Fig. 4 shows frontal sections through the central portion of the thoracic vertebral column of two

15-day-old embryos. On the left is a normal section again. The stage of the so-called mesodermal vertebral column is already passed. The typical metameric segmentation of the primitive vertebral bodies appears. In each segment the caudal half of the sclerotome can be recognized by the particular density of the cells in contrast to the cranial half. The areas of dense mesenchyme, which here have already pushed forward as far as the middle of the myotome, form the anlage for the intervertebral discs. The vertebral body has developed out of the loose mass of sclerotome through expansive growth. This loose mass of

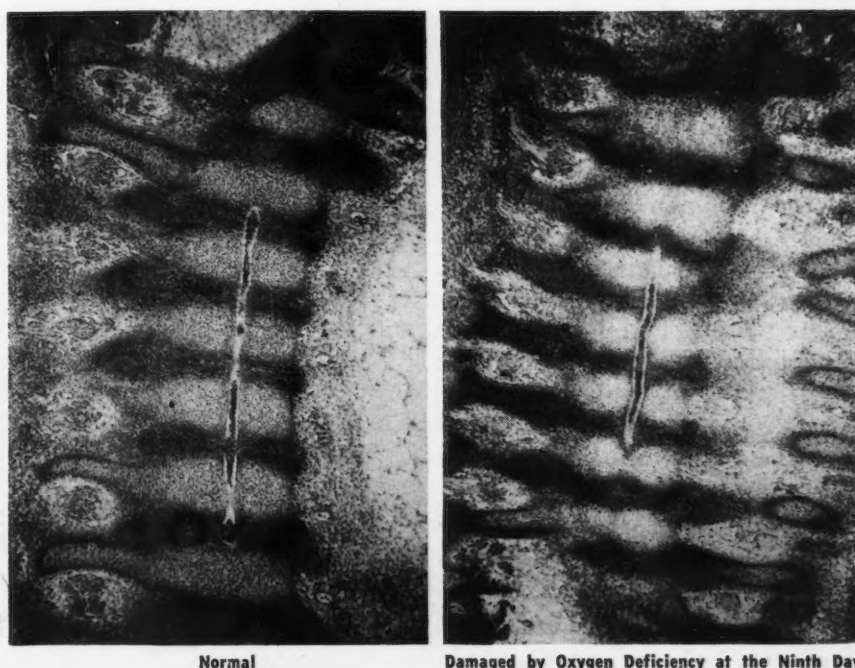
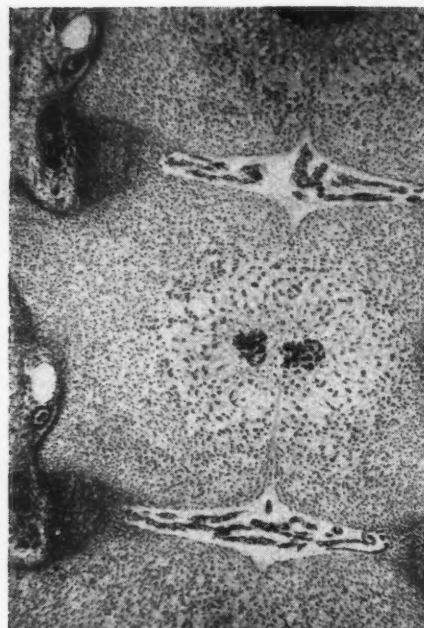
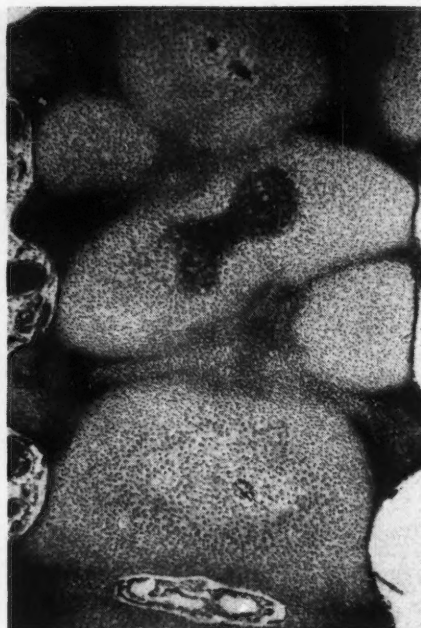


Fig. 4.—Frontal sections through the central portion of the thoracic vertebral column of two 15-day-old embryos.



Normal



Damaged by Oxygen Deficiency at the Ninth Day

Fig. 5.—Frontal sections through the lower thoracic part of the vertebral column of two 2-day-old embryos.

mesenchyme is already in a precartilaginous stage. The picture on the right, however, shows clear aberrations in development of the primitive vertebral bodies. Here again the notochord definitely bends away from the midline. Attention is drawn to the very irregular outlines of the dense mesenchymal masses, both cranially and caudally. This causes an atypical formation of the loose areas of the sclerotome. In the third segment from the top on the left-hand side, the increase of density of mesenchyme of two neighbouring segments has fused into a single complex. In between is a looser, lighter-stained area of mesenchyme which indicates the position of a typically deformed vertebral body. On the left of the picture are two primitive rib-formations rapidly nearing each other. This is the beginning of a typical rib-fork.

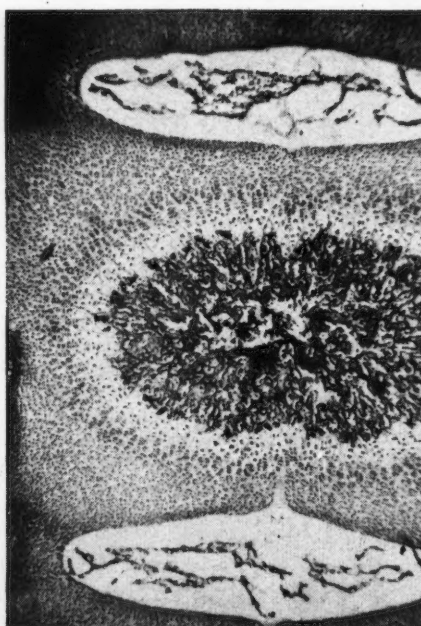
Frontal sections through the lower thoracic part of the vertebral columns of two 21-day-old fetuses show that the stage of the first cartilaginous formation of the vertebral segments is already passed (Fig. 6). On the left is a section of a normal fetus. The first signs of an ossification centre in the primitive vertebral bodies are seen here. The notochord has been largely replaced in this area, but its remains in the areas of the primitive intervertebral discs are regularly arranged. The picture on the right shows severe malformation of the cartilaginous preformed vertebral bodies. At

the top is an asymmetrical, cleft vertebral body, then an atypical small segment follows, showing a thickening of the mesenchyme at the centre and a wedge-formed vertebral body, and below that a relatively normally formed vertebral body with a misshaped cartilage. Notice the malformed intervertebral zones which should have imitated the block formation of all the currently pathological segments.

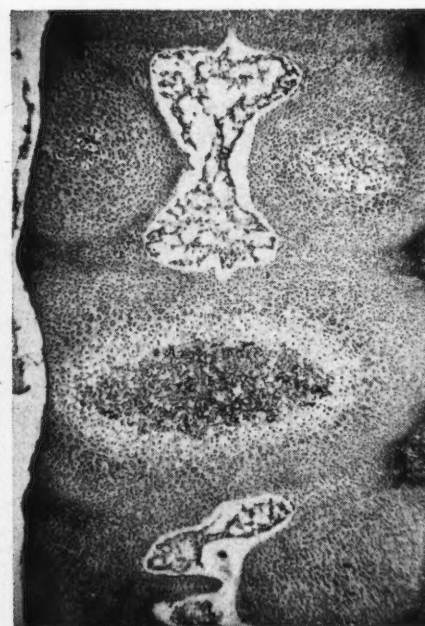
Fig. 6 shows frontal sections of the thoracic vertebral columns of two 25-day-old rabbit fetuses. Ossification of the vertebral bodies has progressed rapidly. On the left is a picture of a normal vertebral body. On the right, one can see considerable structural alterations in the formation of the vertebral bodies. At the bottom is the anlage of a cleft vertebral

body, with a separate centre of ossification in each part. At this point the remains of the notochord in two neighbouring intervertebral discs are still connected in the midline. Above that lies an obviously underdeveloped vertebral body. Above that again lies an asymmetrical, cleft vertebral body.

All these structural alterations are to be traced back, in the main, to damage to the notochord on the 9th day of embryonic development. They agree in detail with the findings of Professor Töndury of Zürich in his investigations into inherited defects in the vertebral column of the Danforth short-tail mouse.



Normal



Damaged by Oxygen Deficiency at the Ninth Day

Fig. 6.—Frontal sections of the thoracic vertebral column of two 25-day-old fetuses.

SUMMARY

Rabbit does were exposed for four hours to severe oxygen deficiency when nine days pregnant. The young regularly showed developmental anomalies of the vertebral column. The histological character of these anomalies is described. They correspond to hereditary defects occasionally seen in mice.

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RÉSUMÉ

Les auteurs ont réussi à créer des anomalies congénitales dans la portée de lapines gravides soumises pendant quatre heures à une atmosphère pauvre en oxygène au cours du neuvième jour de la grossesse. Ces anomalies intéressent constamment la colonne vertébrale et se rattachent aux altérations subies par la notocorde pendant le développement embryonnaire. Elles correspondent aux infirmités héréditaires observées quelquefois chez les souris.

EVALUATION OF THENALIDINE TARTRATE (Sandostene) IN DERMATOLOGICAL DISORDERS*

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MANY SO-CALLED "antihistaminic" and antiallergic preparations are now at our disposal and more are constantly being elaborated. Among the more recent ones, thenalidine tartrate (Sandostene) has attracted our attention on account of its original chemical structure, interesting pharmacology, and a number of promising clinical reports on a total of some 5300 cases. We have therefore made an attempt to evaluate the clinical usefulness of thenalidine, both with respect to the symptomatic relief and the wider therapeutic action that this drug is able to provide in the treatment of various dermatoses and drug reactions.

Thenalidine tartrate (Sandostene) is 1-methyl-4-amino-N'-phenyl-N'-(2'-thenyl)-piperidine tartrate, thus possessing two distinctive radicals (thenyl and methyl-piperidine) not found in other antihistamines. It reportedly possesses a marked anticholinergic and local anæsthetic effect, occupies an intermediary position between the weakest and strongest antihistamines currently used, and is of very low toxicity.¹ It has been demonstrated that in combination with a calcium salt (calcium gluconogalactogluconate) the efficacy of thenalidine is enhanced while toxicity is further reduced.^{2, 6} Calcium salts have been used therapeutically for several decades, although their precise mechanism of action remains unknown; only recently was it demonstrated experimentally that they are able to alter capillary permeability.³ In life with this,

it was found that the combination of thenalidine and calcium gluconogalactogluconate possesses a pronounced antipermeability effect, as evidenced at the hæmato-ocular barrier in man⁴ and by way of the histamine wheal test.^{5, 8}

An exact evaluation of the effect of thenalidine and thenalidine + calcium appears difficult, and a valid quantification can in fact be achieved only by controlled experiments. However, in this investigation we have not run parallel series because we felt it unreasonable to subject patients suffering from acute pruritic conditions to lengthy placebo experiments and to expect their cooperation. Nevertheless, we believe that it was possible to make fairly accurate observations by adhering strictly to certain rules:

1. It is of paramount importance to consider carefully the natural history and prognosis of the condition under observation. For example, one might scrutinize the course of the serum-sickness-like urticarial reaction occurring after penicillin medication. This disorder tends to persist for at least 10 days, if untreated. If therapy is begun at the time of the onset of symptoms and if all symptoms are abolished within 24 hours, it appears permissible to attribute this result to the therapeutic agent used; if, on the other hand, treatment is instituted on the 10th day of the reaction, remission after 24 hours should be considered as probably spontaneous and not due to therapy. Similarly, a chronic skin disorder such as an atopic dermatitis may show spontaneous remissions and exacerbations. Accordingly, the pattern of previous attacks and the whole course of the disease have to be considered carefully before attributing any therapeutic effect to the agent used. Seasonal remissions are common in this disease; therefore thenalidine was tried only during the winter months.

*From the Department of Medicine, Sub-department of Dermatology, Royal Victoria Hospital, Montreal.

TABLE I.—SUMMARY OF RESULTS

Diagnosis	No. of cases	Duration of disease before treatment	Duration of treatment	Method of administration			Results				
				i.v.	i.v. and oral	oral	Excellent	Good	Equivocal	Partial	Failures
Contact dermatitis, (poison ivy; derm. venenata)	23	5 days to many years	4 to 21 days	2	11	10	4	10	3	3	3
Seborrhœic dermatitis	7	2 months to 3 years	14 to 30 days			7	2		1		4
Atopic dermatitis	7	5 months to many years	10 to 28 days	1	12	2	1	4	4	3	3
Stasis dermatitis with eczematization, allergic eczemas, dermatitis of unknown origin	34	2 days to many years	5 to 28 days	6	22	6	17	4	6	2	5
Pruritus: primary, secondary, psychogenic, senile	11	2 months to 2 years	10 to 30 days	4	2	5	0	2	3	5	1
Severe headache following lumbar puncture	2	5 days	2 days	2			2				
Acute urticaria	12	5 to 10 days	2 to 10 days	2	2	8	4	4	2		2
Chronic urticaria	13	2 months to 10 years	2 to 24 days	4	5	4	3	4	1	4	1
Purpura of Majocchi	1	2 months	1 month		1			1			
Drug eruptions	12	2 to 20 days	2 to 14 days	5	6	1	6		4	1	1
Erythema multiforme	1	14 days	5 days			1	1				
	131			26	61	44	40	29	24	18	20

2. The suggestive effect of any new therapy, particularly that of intravenous injections, has to be taken into account. We were unable to rule out the possible suggestive effect in some of our patients; however, the majority of them have had numerous forms of treatment, including injections, thus reducing the suggestive hazard to a minimum.

3. Any investigator of new drugs should be sceptical; we tried to maintain this state of mind throughout the investigation.

MATERIAL AND METHOD

The case material (131 patients) was chosen from the out-patient department of the Skin Clinic of the Royal Victoria Hospital and from the private offices of its staff members. The drug under investigation was supplied in coated tablets containing 25 mg. of thenalidine tartrate, and in ampoules of 10 ml. injectable solution containing 50 mg. of thenalidine and 1.375 g. of calcium glucogalactogluconate.

Patients were treated orally and/or parenterally in one of the three following ways with: (1) daily i.v. injections of 10 ml.; (2) twice weekly injections of 10 ml. plus 2 tablets four times daily on the days when no injections were given; (3) 2 tablets orally four times daily. As patients improved, dosage was stepwise reduced to 4 tablets daily. In a few acute cases, injections were given at intervals of eight hours.

RESULTS

Table I summarizes and classifies our results according to the criteria mentioned above. Results

were considered (1) *excellent*—if the therapeutic effect was complete and could be unequivocally attributed to the agent under investigation; in the case of chronic relapsing conditions, if no relapse occurred within a three-month medication-free follow-up period; (2) *good*—if the observed improvement was unquestionably due to the drug, but control was not quite complete and minor relapses occurred occasionally during the medication-free observation time, provided these relapses could be controlled by reinstitution of therapy; (3) *equivocal*—if satisfactory response was recorded but it could not be ascertained whether the observed improvement was due to the drug or to other factors, such as spontaneous remissions, suggestion, or the effect of concomitant topical therapy; (4) *partial*—if the therapeutic effect consisted in symptomatic relief from pruritus only, without influencing the course of the disorder; (5) *failures*—if little or no response to medication was noted.

COMMENTS

Of a total of 131 patients, 26 (20%) were treated by i.v. injection only, 61 (47%) received combined oral and parenteral medication, and 44 (33%) were given tablets only. The most rapid results were achieved by daily injections of 10 ml. (or more) of thenalidine + calcium. The highest percentage of excellent or good results was obtained in urticarial and drug eruptions; only transient results were achieved in seborrhœic and atopic dermatitis. The duration of treatment was determined for each case according to need

and ranged from 2 to 30 days. Treatment was discontinued if no improvement occurred within four weeks.

Side effects such as dryness of the mouth, tiredness or drowsiness were infrequent and were, with the oral treatment, of such mild and transient nature that they required no further attention. Drowsiness occurred occasionally after parenteral administration of Sandostene. However, when deemed expedient, as in the case of taxi drivers, this was easily controlled by administration of a central nervous stimulant (e.g. 5 mg. of Dexamyl) before the injection was given. To our knowledge, there are no special contraindications. However, digitalized patients and patients with malignant hypertension should not be treated parenterally.

During the course of this investigation an article was published in the *Journal of the American Medical Association*⁷ concerning three episodes of agranulocytosis in allergic patients of long standing who had been treated with various drugs, including thenalidine tartrate (Sandostene). Seeing that similar reports have already appeared on a number of widely used antihistamines, we felt prompted to re-examine our case material treated so far (131 cases) and to follow closely the blood picture in 20 cases during and after treatment. In one case only did we notice a moderate drop of the white cell count from 6800 to 5000 per c.mm. and, without reduction in the dosage of thenalidine, a subsequent rise to 5600 per c.mm. after two weeks of treatment. No complaints indicative of an altered blood picture could be elicited from any patient. From the outset we reserved the use of thenalidine for a limited length of treatment, not to exceed three months. This would seem to reduce any alleged danger of untoward reactions, to which the patient in need of an antihistamine seems to be intrinsically prone.

ILLUSTRATIVE CASES

CASE 1.—P.S., a 20-year-old man, developed a severe reaction eight days after a penicillin injection. He suffered from general malaise, a temperature of 103-104° F., and difficulty in breathing and swallowing. He was covered with widespread giant urticaria. Therapy was instituted at once and all symptoms subsided abruptly after two injections of thenalidine, given eight hours apart. The patient was discharged free of symptoms, 48 hours after start of therapy.

CASES 2 and 3.—C.S. and P.A., 40- and 48-year-old women, had been suffering from an acute inflammatory perianal and perigenital dermatitis for two years. Both women complained particularly of painful premenstrual exacerbations. Blood sugar studies and vaginal and cervical smears revealed only the usual flora, and no parasites were found in the stool. Apart from neurotic symptoms and anxiety, no abnormalities were found. Previous therapy with numerous agents had proved unsuccessful. A course of 16 injections of thenalidine, given twice weekly and combined with oral treatment (2 tablets 4 times a day) on the days when no injection

was given, resulted in a marked improvement. No relapse had occurred at the end of the observation time, two months after cessation of all therapy.

EVALUATION OF THENALIDINE IN OFFICE PRACTICE DURING A FIVE-YEAR PERIOD

Apart from the preceding clinical evaluation thenalidine has been used by one of us (L.P.E.) during a five-year period for the treatment of a wide variety of pruriginous dermatoses met with in our office clientele. The results in over 500 cases treated with thenalidine were appraised. While claims for its therapeutic specificity are not advanced from the results obtained in this series, it can nevertheless be stated that it was found to be a most useful antipruritic agent and an excellent therapeutic adjunct in general dermatological therapy as a means of giving comfort to our patients.

In our hands, thenalidine has been a safe agent, carrying with its action a minimum of side effects. In common with other antihistaminic and anticholinergic drugs, it possesses the potential of causing nausea, dizziness, dryness of the mouth and drowsiness. Mild reactions of this type were occasionally encountered after the first administration of thenalidine, but they were transitory in nature and usually disappeared well within 48 hours when a dosage schedule was maintained or reduced. In the whole group no instances of serious reactions were encountered, and no disorders referable to the hæmatopoietic system were discovered. Nevertheless we concur with the recommendations by Garbe⁹ that patients report immediately any untoward signs, and that blood counts be taken where patients are on prolonged antihistamine treatment. Our own treatment with thenalidine has not exceeded a period of three months.

The tablets of thenalidine (Sandostene) possess an added advantage in that they are free of dyestuffs frequently employed in the colouring of drugs. A recent paper from France¹⁰ warns of the urticaria-provoking properties inherent in some of the coloured antihistaminic tablets currently available in that country.

A useful routine was developed for the cases suffering from chronic pruritic skin disorders. This consisted of a 50 mg. dosage schedule, one tablet of thenalidine being taken after the evening meal and a second at bed time. Invariably, these patients had a comfortable night's rest. Intravenous therapy, 10 ml. of "thenalidine + calcium" once daily for three days, was reserved for the acute urticarias, acute eczematous processes, acute dermatitis venenata, acute drug reactions and for the exudative types of erythema multiforme. At the end of this period, maintenance doses of 75 to 100 mg. (3 to 4 tablets) per day were given.

CONCLUSIONS AND SUMMARY

Thenalidine tartrate (Sandostene) was given a therapeutic trial in 131 patients suffering from various forms of dermatitis and of urticaria. Results have been carefully scrutinized and evaluated. Complete therapeutic success was achieved in 30.5% of cases, results were good in 22.2%, equivocal in 18.3%, partial in 13.7% and absent in 15.3% of patients. Setting aside our critical classification, it can be stated that good results were obtained in 71.0% of cases, fair results in 13.7% of cases, and no result in 15.3% of cases.

From an evaluation of over 500 cases in office practice during a five-year period, thenalidine tartrate was found to be an effective adjunct in general dermatological therapy.

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RÉSUMÉ

Les auteurs présentent leur évaluation de la thérapeutique au Sandostène (*marque déposée*) telle qu'observée chez 131 malades porteurs de formes diverses de dermatite et d'urticaire. Une réussite complète fut obtenue dans 30.5% des cas; les bons résultats s'élevèrent à 22.2%, les résultats équivoques à 18.3% et les partiels à 13.7%. Aucun effet ne fut noté chez 15.3% des malades. Grosso modo, les bons résultats atteignirent 71%; on compta 13.7% de résultats acceptables et il y eut échec dans 15.3% des cas.

D'après les quelque 500 cas de ville dans lesquels, au cours d'une période de cinq ans il fut administré, le Sandostène se rangea parmi les auxiliaires efficaces de la thérapie dermatologique.

ALTERATION OF WHEEL RESORPTION TIME BY INTRAVENOUS USE OF AN ANTI-HISTAMINIC DRUG AND A CALCIUM SALT*

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BOTH CALCIUM and antihistaminic drugs are supposed to decrease vascular and membrane permeability, although they act on different sites. Evidence for this and for an apparent synergism between these two types of drugs has been brought to light by a number of investigations.¹⁻⁵ We nevertheless felt prompted to re-examine this question with the help of different methods and preparations, on account of its practical importance.

We used wheal resorption time (a modified McClure-Aldrich test) for measurement of the effects of thenalidine tartrate (1-methyl-4-amino-N'-phenyl-N'-(2'-thenyl)-piperidine tartrate) and calcium gluconogalactogluconate, injected intravenously, both singly and in combination (Sandostene + calcium).

MATERIAL AND METHOD

1. To normal saline solution hyaluronidase was added in order to decrease the absorption time. A solution of 50 TRU of hyaluronidase in 1.0 c.c. of saline was used to produce the test wheals. Of this solution 0.1 c.c. was injected intradermally into the skin of the upper back between the angle of the scapula and the spine. Three wheals were produced on one side of the back of each subject, and the

time required for complete disappearance of the wheals was recorded.

2. After complete disappearance of the wheals, 10 ml. of the drugs to be tested was injected intravenously. The three drugs used were: (1) a solution of 1.375 g. of calcium gluconogalactogluconate in 10 ml. water, equivalent to a 10% solution of calcium gluconate (Calcium-Sandoz 10%); (2) a 5 mg. per ml. aqueous solution of thenalidine tartrate (Sandostene); (3) a solution of 50 mg. of thenalidine tartrate in 10 ml. of Calcium-Sandoz 10% (Sandostene + calcium). The thenalidine + calcium was given to 14 subjects. Calcium-Sandoz 10% and thenalidine were each given separately to five subjects. All three drugs were given intravenously.

3. Fifteen minutes later a second series of three wheals was made in the above-described manner on the contralateral side of the spine, and the time until their complete disappearance was recorded.

RESULTS

1. The wheal resorption time was significantly shortened in 13 of the 14 patients to whom then-

TABLE I.—WHEEL RESORPTION TIME IN MINUTES BEFORE AND AFTER I.V. THENALIDINE + CALCIUM INJECTION

	Before			After		
1	27	27	27	20	21	21
2	41	41	41	34	34	34
3	37	37	37	31	31	31
4	32	33	33	27	27	23
5	30	30	30	27	27	27
6	26	25	26	20	19	21
7	52	52	52	43	43	43
8	41	41	40	26	26	26
9	33	33	30	26	27	26
10	29	30	30	23	21	23
11	37	37	39	32	31	31
12	27	27	28	23	22	22
13	43	43	43	38	39	38
14	38	39	38	38	38	37

Subjects 1 to 11 were free of skin diseases. Nos. 12 and 13 were psoriatics. Subject 14 had completed a series of ultra-violet treatments three days before the experiment.

*From the Department of Medicine (Section of Dermatology), Royal Victoria Hospital, Montreal. This investigation was supported by a grant given by Sandoz (Canada) Ltd., who also supplied the materials used.

TABLE II.—WHEEL RESORPTION TIME IN MINUTES BEFORE AND AFTER I.V. THENALIDINE INJECTION

	Before			After		
1	43	43	49	43	45	49
2	31	31	31	26	26	28
3	19	20	19	17	17	17
4	27	30	27	25	25	24
5	27	27	27	20	22	22

alidine plus calcium was given. Case 14 had recently been given large doses of ultraviolet light in combination with tar ointments, which may have been a factor in the relative lack of response.

2. No significant alteration occurred after administration of the calcium salt alone.

3. Thenalidine alone caused a shortening of the wheal resorption time in four out of five cases.

STATISTICAL EVALUATION

1. Thenalidine, with and without calcium, significantly reduced wheal resorption time ($P < 0.001$), but calcium alone produced no significant change ($P > 0.20$).

2. Thenalidine with calcium had a significantly greater effect than thenalidine alone ($0.01 > P > 0.001$).

3. There was no significant difference between the pre-treatment values of the three different substances tested ($P > 0.20$).

4. There was no significant difference between the first and second series of wheals, or between the first and third, and the second and third series ($P > 0.20$).

DISCUSSION

Antihistamines have been shown to act on capillary permeability by their effect on precapillary sphincters. One might also consider the possibility that an antihistaminic drug may act upon histamine released in the test area by needle trauma; however, Stewart and Bliss⁶ found in experiments with diluted human plasma that addition of an antihistaminic to their test solution did not alter the wheal response.

Calcium has been shown to affect intracellular cement substance of capillaries and to act on cell membranes, changing the ionic balance and the colloid hydration. Calcium salts have been used therapeutically in allergic inflammatory disorders since Wright's report in 1898; experimental evidence for the effectiveness of calcium in this respect has been published only recently. Heite and Schrader⁴ observed a shortening of the wheal resorption time after intravenous calcium medica-

tion. Our experiments do not support their findings, but it should be pointed out that our techniques were not the same. Huber² demonstrated an alteration of the permeability at the hæmato-ocular barrier in the human eye after calcium administration. Cerletti and Rothlin^{1,3} reported on the synergistic effect of antihistamines and calcium; it is possible that the effects observed in our series were due to such an additive effect of the two drugs. While calcium alone did not alter the wheal resorption time in our experiments, the addition of calcium to thenalidine increased the effect of the latter significantly. The mechanism of wheal resorption is complex, and the speed of fluid resorption could be altered by at least two factors: (1) alteration of diffusion rate of the injected fluid into the interstitial spaces; (2) alteration in speed of fluid absorption into blood and lymph vessels.

In living animals, fluids move across membranes constantly and in both directions. Apart from the well-known forces governing inflow and outflow, such as hydrostatic and osmotic pressures, one may consider a membrane as a metabolic entity. Changes in the living cell may alter outflow rate or retrograde flow rate, or both. Hence, wheal resorption time could be decreased by reduction in outflow or by an increased retrograde flow, or both. Which of the components of this dynamic situation was altered in our experiments we do not know.

SUMMARY

A solution of an antihistamine (thenalidine tartrate) and of a calcium salt (Sandostene + calcium) was given intravenously in order to measure its effect on wheal resorption time.

A decrease of about 20% in wheal resorption time was recorded after administration of this drug. No decrease was found when calcium alone was used, while the antihistaminic alone was effective, but less so than when given in conjunction with calcium.

The statistical evaluations were done by Dr. B. Grad, Allan Memorial Institute, Montreal.

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RÉSUMÉ

L'auteur a cherché à déterminer le degré de renforcement pharmacologique que peut offrir un sel de calcium à l'action d'un anti-histaminique. Le produit employé fut le Sandostène avec calcium. On compara le temps de résorption d'une efflorescence cutanée de sensibilisation, spontanément et sous l'influence de l'un ou l'autre de ces médicaments. Lorsque les deux furent employés simultanément cette période fut raccourcie de 20%. L'administration de calcium seul n'eut aucun effet, alors que l'anti-histaminique seul améliora quelque peu la situation sans toutefois atteindre le degré d'efficacité mentionné ci-dessus.

TABLE III.—WHEEL RESORPTION TIME IN MINUTES BEFORE AND AFTER I.V. CALCIUM INJECTION

	Before			After		
1	30	30	30	30	31	30
2	28	28	28	30	30	31
3	27	27	27	23	23	23
4	39	39	39	40	40	40
5	34	34	34	32	32	32

Case Reports

INTRAVASCULAR HÆMOLYSIS AND ACUTE RENAL FAILURE FOLLOWING POSTABORTAL SEPSIS DUE TO CLOSTRIDIUM WELCHII

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Clostridium welchii is an uncommon cause of postabortal or puerperal sepsis, in spite of reports indicating that the organism may be recovered from the vagina in 4 to 6% of normal pregnant women.^{1,2} In part, this rarity of severe infection is due to the fact, first shown by Welch,³ that the bacillus requires dead or damaged tissue in which to multiply. In addition, the highly virulent variants, of the type responsible for fulminating infections, form only a small minority of the several hundred strains that have been isolated.⁴

The clinical course of infection varies widely from cases in which there is local gas gangrene, with or without metastatic abscess formation, to those in which septicæmia, cardiovascular collapse and evidence of intravascular hæmolysis predominate. Butler⁴ has found a definite relationship between the severity of human infection and the ability of the particular strain of *Cl. welchii* involved to produce alpha toxin and to resist phagocytosis by human leukocytes. Mortality is high, ranging from 40 to 70%,⁵⁻⁷ and appears to have been but little modified by the use of antitoxins. In patients surviving the first few days, acute renal failure, secondary to massive intravascular hæmolysis, has been a major cause of death.⁵⁻¹³ The following report details some of the problems encountered in the management of a case of postabortal sepsis with intravascular hæmolysis due to *Cl. welchii*.

A 36-year-old rural housewife was seen on June 16, 1958, during the fourth month of her second pregnancy, at which time she was perfectly well. Blood pressure was 120/80 mm. Hg; urine and hæmogram were normal. On the afternoon of June 21, while she was hanging up the washing, the membranes ruptured; there was no pain or bleeding. The following morning she felt feverish, went back to bed and began to bleed profusely per vaginam. She had a chill and her temperature rose to 102° F. On admission to hospital at 1.00 p.m. she was pale, lung fields were clear, blood pressure was 98/60 mm. Hg and pulse rate 72. The abdomen was tense and tender, uterus enlarged about the size of a four-month pregnancy and there was moderate vaginal bleeding. She aborted at 3.00 p.m.; the expelled fetus was severely macerated. After

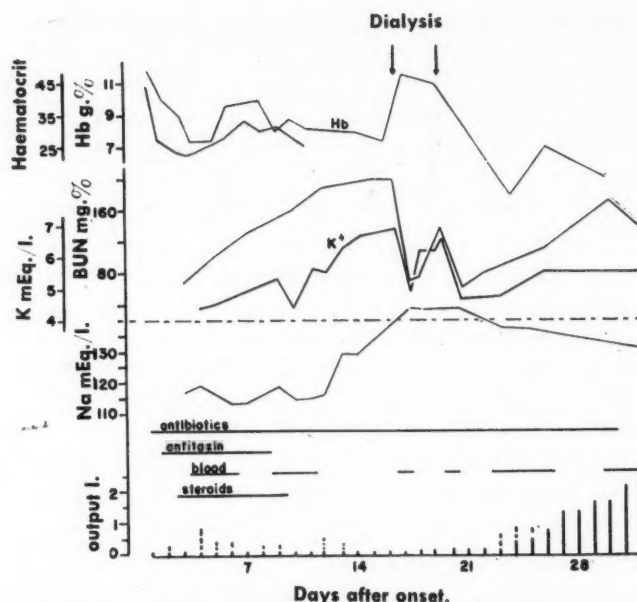


Fig. 1.—Changes in hæmoglobin, hæmatocrit and blood chemistry during oliguria and early diuresis in patient with acute renal failure. The interrupted horizontal line represents normal values in this laboratory for the biochemical parameters shown.

delivery it was noted that her colour was darker and it was thought that perhaps she was becoming jaundiced. Penicillin administration was begun. A catheter urine specimen, 30 ml. in volume, was deep red, contained 4% protein and showed only the occasional red blood cell per high power field on microscopic examination. Sections of the expelled fetus showed numerous large bacilli in skin and muscle, subsequently identified as *Cl. welchii*. The placenta, which was incompletely passed, showed no microscopic evidence of bacterial infiltration.

By June 23, the patient was a dusky bronze colour and the blood serum showed gross hæmolysis. Despite evident hæmolysis the patient's general condition remained fairly good; blood pressure was between 90/50 and 100/60 mm. Hg, pulse rate was 100, and peripheral circulation appeared to be adequate. Following the report that the fetus showed clostridial organisms, chloramphenicol (Chloromycetin) (1 gram a day), hydrocortisone (100 mg. a day) and gas gangrene antitoxin (30,000 to 60,000 units a day) were begun.

The patient remained oliguric (less than 200 ml./24 hr.) for 23 days, from June 22 to July 15. During this period she was maintained on a basic daily intravenous intake of 0.6 to 0.8 litre of 50% glucose (given via indwelling catheter in the subclavian vein) to which was added sodium as M/6 lactate, amounts being dictated by her losses due to diarrhoea and vomiting. At the onset of hæmolysis, the hæmatocrit value fell rapidly to 24%, hæmoglobin to 7 g. per 100 ml.; the reticulocyte count was 5% and there were normoblasts in the peripheral blood smear. The platelet count was only 3500 and a leukocytosis to 25,000 was observed. Liver function tests showed abnormal flocculations. Multiple transfusions of fresh packed cells, some from siliconed containers, were given. Timing and amount of blood given were dictated primarily by the circulatory status and hæmatocrit value. The serum remained burgundy-coloured for the first four days and hæmoglobinuria persisted for somewhat longer.

By July 2, the patient had become confused, was irrational at times and showed evidence of increased

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neuromuscular irritability which was not improved by intravenous calcium. Because of deterioration in clinical status and progressive rise in serum potassium level, she was subjected to a six-hour period of *in vivo* dialysis on July 8. This procedure was accompanied by a fall in serum potassium from 6.8 to 4.9 mEq./l. and the blood urea was coincidentally reduced from 185 to 70 mg. % (Fig. 1). Little clinical change was evident during this dialysis. However, by the time of the second dialysis two days later, she was rational and neuromuscular irritability was near normal. On this occasion a six-hour period of dialysis was accompanied by a fall in serum potassium from 6.6 to 4.6 mEq./l. and blood urea from 136 to 68 mg. %. Vaginal bleeding, which had been present for most of the stay in hospital, became more marked, and on July 14, a dilatation and curettage was done with the removal of a fair quantity of degenerated decidua. Examination of vaginal smears and of material removed by curettage did not show any clostridial organisms. Positive blood cultures were never obtained. Spontaneous diuresis began on July 15. A renal biopsy on August 8 showed changes characteristic of acute renal ischaemia (Fig. 2).

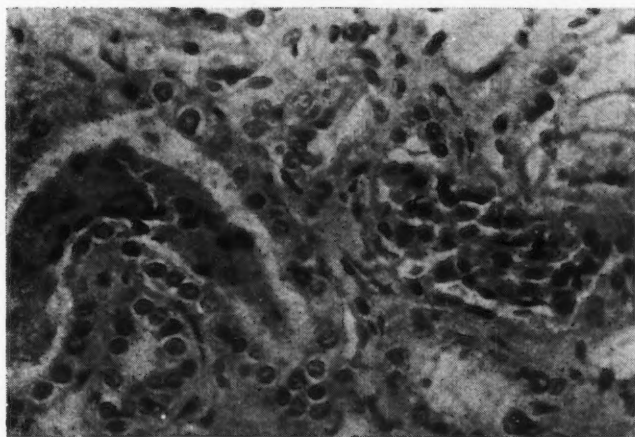


Fig. 2.—Microscopic picture of renal biopsy specimen showing epithelial casts and atrophic tubular epithelium. Interstitium shows chronic inflammatory cells and oedema. $\times 200$.

Convalescence was complicated by an effusion into the left elbow joint on August 21. Culture of joint fluid grew *Staphylococcus pyogenes*, coagulase positive, and antibiotics were administered again for a period. The diuretic phase of the renal failure was prolonged. Urine volumes remained in excess of 3 litres per day from August 3 to September 2; urine specific gravity was relatively fixed at 1.012 during this period, and sodium and potassium concentrations remained at or about 80 and 20 mEq./l. respectively. The blood urea did not fall to normal levels until August 26. Some measure of returning renal function was shown by serial determinations of endogenous creatinine clearance which rose slowly from a level of 4 ml. a minute on July 23 to 36 ml. a minute on September 10. The patient was discharged from hospital on September 10, and has since resumed her duties as a housewife.

COMMENT

The treatment of *Cl. welchii* infection is usually directed towards destruction of the invading organism and general supportive measures during the period of toxæmia. The bacillus is sensitive to

penicillin,¹⁴ and most authors agree that this drug is clinically effective when given early. The value of antitoxin is less well established, possibly because this diagnosis is not often suspected in post-abortal or puerperal sepsis until the development of hæmolysis. By this time, the destruction of the cellular elements of the blood is already great. In addition, *in vivo* resistance to phagocytosis of the organism has been shown to be practically unaffected by the presence of antitoxin.⁴

Most published reports stress the hæmolytic aspects of *Cl. welchii* septicæmia. However, little attention has been paid to the accompanying hæmorrhagic phenomena which have been demonstrated in the experimental animal following intravenous injection of alpha toxin.^{15, 16} These are:

1. Early and precipitous fall in platelet count.
2. Increase in coagulation time.
3. Hypoprothrombinæmia and hypofibrinogenæmia.

Human autopsies showing multiple hæmorrhages in organs and hæmorrhagic serous effusions attest the importance of this hæmorrhagic diathesis. Whether the early use of steroids and of fresh packed red cells influenced the outcome in the present case must remain uncertain; however, no bleeding other than from a retained portion of the placenta was observed. The platelet count, which was 3500 per c.mm. on the first examination, returned to levels above 150,000 soon after steroids were begun. Unfortunately, prothrombin time and fibrinogen levels were not determined before transfusion and administration of steroids. When checked before dialysis, these parameters were normal.

Renal ischaemia and the subsequent development of acute renal failure was most likely due to the pressor effect of free hæmoglobin which has been shown to follow experimentally induced hæmolysis.¹⁷ Evidence of this pressor effect, as reflected by peripheral vasoconstriction and rise in blood pressure with narrowing of pulse pressure, frequently observed in other cases of hæmolysis, was not recorded in the present case. This may have been missed because of its early occurrence or have been masked by the febrile onset of the illness. The use of *in vivo* dialysis in acute renal failure due to this cause has been reported on two previous occasions. In a case recorded by Dique,¹¹ dialysis was employed on the 10th day of oliguria; diuresis began on the 14th day and the patient recovered. In another instance, reported by French,¹³ dialysis was employed but the patient did not survive. In the present case, early evacuation of the uterus and control of infection likely played a part in the relatively slow biochemical deterioration during oliguria. Although dialysis was accompanied by marked clinical and biochemical improvement, it is unlikely to have influenced the ultimate occurrence of diuresis. Electrolyte losses were not excessive during the prolonged diuresis and could readily be balanced

by appropriate dietary adjustments. It is likely that this woman will have a diminished renal functional capacity for some months to come.

SUMMARY

A case of postabortal sepsis due to *Cl. welchii* is presented.

The use of *in vivo* dialysis as an adjunct to conservative management is discussed.

The authors wish to thank Dr. K. Borthwick-Leslie for referring this patient. Dr. Leslie's prompt recognition of the etiology and early institution of antibiotic and steroid therapy undoubtedly contributed to the successful outcome.

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IDIOPATHIC HYPERCALCAEMIA OF INFANCY*

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IDIOPATHIC infantile hypercalcaemia occurs in two forms, "mild" and "severe". With the former, originally described by Lightwood and by Payne,¹ previously healthy infants become ill with anorexia, vomiting, wasting and constipation, usually between three and seven months of age. Clinically it is not possible to distinguish these patients from those suffering from primary renal acidosis and other causes of "failure to thrive" in infancy. Blood biochemical studies reveal no acidosis, however, but a raised serum calcium with normal phosphorus and alkaline phosphatase levels. The prognosis of these cases is usually good. The severe form of the disease was first described by Fanconi *et al.*² In addition to the features of the mild type these patients show physical and mental retardation, a characteristic facies, precordial systolic murmur, frequently hypertension and osteosclerosis; the majority eventually die before the age of three years, usually from renal insufficiency. There is

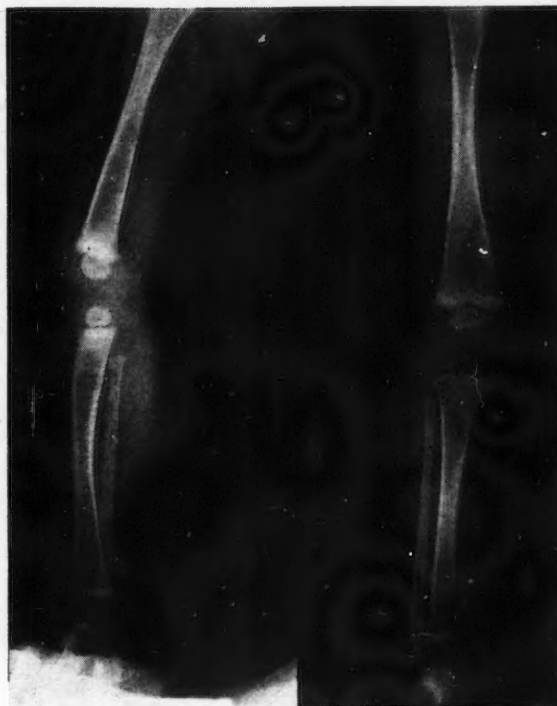


Fig. 1.—Radiograph of right leg at 8 months of age.

some overlapping of the features characteristic of the mild and severe types³ and it seems likely that they are really different degrees of the same disease.

Most cases of infantile hypercalcaemia have been reported from Europe but recently there have been a few case reports from the United States.⁴⁻⁷ The disease appears to be less common on the North American continent,⁸ and as far as I am aware no case has hitherto been reported from Canada. The following report of a case of the severe form of the disease is therefore considered justified.

A baby girl (E.E.), who lived in rural Manitoba, was born after a normal pregnancy and delivery and her birth weight was 7 lb. 3 oz. (4030 g.) The parents are healthy and not related. There are two siblings, aged four and three years, who are apparently healthy except that the elder child has congenital nystagmus. The only other relevant fact in the family history is that the mother's sister had had a baby who died shortly after birth with multiple skeletal abnormalities.

E.E. was slow to feed at first but was eventually established on a cow's-milk and water formula which she took well. Initially the milk was diluted with equal parts of water and this feed was gradually strengthened until, just before her illness began, she was receiving 38 oz. (1080 c.c.) milk and 2 oz. (57 c.c.) water per day. Solids were started at two months of age and she was given five drops of Ostoco daily (1000 international units vitamin D), but this was never taken well. When two months old, she had a minor respiratory infection which responded quickly to treatment with penicillin. At four months she weighed 13½ lb. (6123 g.) and immunizations were started; at six months she was able to sit without support. At seven months she developed bronchitis which was treated with penicillin. At this time she was

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TABLE I.—SUMMARY OF BIOCHEMICAL FINDINGS

	*								
Age in months	8	8½	9½	10*	12	13	16*	17	22
Calcium (mEq./l.)	7.4	5.6	6.6	5.8	5.8	5.9	3.0	4.1	
	6.1								
Phosphorus (mEq./l.)	3.3						3.3		
Blood urea nitrogen (mg./100 ml.)	43.0	21.2	27.0	32.0			15.6		
Cholesterol (mg./100 ml.)	240.0	210.0	128.0	164.0					
Proteins (g./100 ml.)	7.2						4.32	6.8	
Albumin	5.1						3.04		
Globulin	2.1						1.28		
Hæmoglobin (g./100 ml.)	10.8			12.5			7.9	10.9	14.3

*Indicates the period the patient was in hospital.

noticed to be very hypotonic and could no longer sit unsupported. Three weeks later her chest was clear, but she was wasted and lethargic, and a cardiac murmur was heard for the first time. From then onwards she continued to deteriorate and was intermittently febrile, irritable and constipated. She vomited and was very difficult to feed. Urine contained pus and casts but was sterile on culture. She was admitted to the Children's Hospital, Winnipeg, when eight months old.

Examination on admission showed a very ill baby who was wasted and moderately dehydrated. Her rectal temperature was 102° F. and she weighed 12 lb. Faecal masses were palpated through the abdominal wall. She had a convergent squint, but nothing remarkable was noted about the facies. She had generalized muscular hypotonia and was unable to sit unsupported, and head control was poor. Tendon reflexes were all present and normal. A blowing systolic murmur was heard over the whole precordium, maximal down the left border of the sternum, but the heart was not enlarged and the blood pressure was normal.

Investigations.—Hæmoglobin value 10.8 g. %; leucocytes 6700 per c.mm. with a normal differential count. Several specimens of urine were examined and were all normal except that specific gravities were constantly below 1.010. Serum bicarbonate, sodium, chloride and potassium were normal; alkaline phosphatase was 4.7 K.A. units. The serum calcium, blood urea nitrogen, and cholesterol were elevated as shown in Table I, where the results of analysis of other blood constituents are also summarized. Radiographs of the skeleton showed that the epiphyses at the knee joint had dense outer margins, 2 and 3 mm. in width, but the central portions were normal (Fig. 1). The ends of the shafts of the long bones were a little more dense than normal. There was minimal increased density at the base of the skull and in the vertebral bodies. Intravenous pyelography was performed but the renal outlines were not demonstrated. Chest radiographs and an electrocardiogram were normal.

Through the courtesy of Mr. W. M. Ward of the Manitoba Department of Health and Public Welfare, a sample of the well water from the farm on which she lived was analyzed, with the following findings:

Calcium	160 parts per million
Magnesium	68 parts per million
Total hardness (CaCO ₃)	690 parts per million

After admission the child was rapidly hydrated with oral fluids, and the temperature became normal after

a few days. She was then given a low calcium diet, and, because initially it was not possible to obtain a low calcium milk, this was achieved by using a strained-meat formula which contained 12 mg. of calcium per pint (568 ml.). This she took well. No vitamin D was given. After receiving this diet for two weeks she gained a little weight, and became much less irritable and more playful and interested in her surroundings. The serum calcium had fallen to 5.6 mEq./l. and the blood urea to normal (see Table I). She was discharged home after having been in hospital for four weeks. The parents were instructed to continue using the meat-milk formula, to avoid milk or milk products, to give only small amounts of meat, fish and cereal, and to use distilled water instead of the local well water.

She was seen again two weeks later, when the mother reported that she seemed to be much better and was eating well. There was no vomiting and she was having normal bowel movements, but she was still very wasted and hypotonic. She seemed interested in her surroundings and could reach and grasp objects. The systolic murmur seemed to be of diminished intensity. At this time she weighed 14 lb. (8060 g.). A month later, when she was ten months old, there seemed to be little further progress and she had gained only two ounces (57 g.) in weight. She had a mild bronchitis and was readmitted to hospital where the bronchitis responded to treatment with penicillin. Prednisone was then started with an initial dose of 20 mg. per day reducing to 10 mg. per day. After a week in hospital she was again discharged home. Laboratory findings on this admission are summarized in the table, the serum calcium being only slightly elevated. Shortly after going home she developed a mild gastroenteritis which subsided after treatment with neomycin.

At the age of one year she weighed 14 lb. 9 oz. (8316 g.) and was 29½ in. (75 cm.) in length. She was still very hypotonic and was unable to sit without support but could raise her trunk off the couch. She seemed happy and playful. The serum calcium was only slightly elevated (see Table I). The systolic murmur could no longer be heard but the squint was still very obvious. At this time a low calcium milk, Locasol,* was started and prednisone was continued with a daily dosage of 10 mg. There was little change in her condition for the next two months; she then developed measles and the prednisone was discontinued. When she was 16 months of age she became ill with vomiting, anorexia and loss of weight, and

*Supplied by Trufood Limited, England. Calcium content not more than 56.8 mg./pint.

swelling of the hands and feet was noticed. She was readmitted to the Children's Hospital, Winnipeg; on admission she looked very ill, was anaemic and wasted and had a temperature of 102° F. There were septic lesions on the eyelids, and excoriated buttocks. Muscular hypotonia was extreme and there was pitting oedema of the face and extremities. At this time it was noted that she had the typical "elfin" facies of hypercalcaemia with thick lips and underdeveloped bridge of nose and mandible (Fig. 2). The systolic murmur was again easily audible and the systolic blood pressure was 85 mm. Hg.



Fig. 2.—Appearance of E.E. at 16 months of age.

Investigations.—Hb. 7.9 g. %. The red blood cells were microcytic and hypochromic. The serum calcium and protein levels were low, as shown in Table I. Urine was normal and on one occasion was concentrated to a specific gravity of 1.036. Radiographs of the abdomen showed no nephrocalcinosis and those of the bones showed some suggestion of osteoporosis. The increased density at the ends of the shafts of the long bones had disappeared.

She was treated with intramuscular penicillin and the temperature settled within 24 hours. The low calcium milk was continued but she was otherwise given a normal diet. The oedema rapidly subsided and the skin lesions healed. She was discharged home after two weeks on a high protein diet, low calcium milk and iron supplements. A month later there was very considerable improvement. She weighed 17 lb. 10 oz. (8 kg.) and was eating well, and there was no sign of oedema. Hb. was 10.9 g. % and total serum proteins 6.8 g. %. When she was 19 months she began to sit without support but was still hypotonic. The cardiac murmur had again disappeared.

She was last seen by us at the age of 22 months when she weighed 19 lb. 13 oz. (8.9 kg.), and her length was 29½ inches. She was a happy and contented baby, able to say "Mummy" and "Daddy", and was beginning to creep but made no attempt to pull herself on to her feet. The squint and "elfin" facies were still very obvious. At this time it was decided that the low calcium milk should be discontinued and a normal diet introduced.

DISCUSSION

E.E. showed most of the features of the severe type of idiopathic hypercalcaemia although hypertension was never observed. During the first hospital admission she showed evidence of renal insufficiency with raised blood urea level and inability to concentrate urine. The blood urea level however rapidly fell (partly perhaps because of rehydration) and during the last hospital admission she was found to be able to concentrate her urine normally. It therefore appeared that the kidneys had "recovered". The low calcium diet was effective in reducing the serum calcium, although at 13 months of age there was still slight hypercalcaemia, and it may be assumed that treatment was started in time to prevent irreversible renal damage but not in time to prevent permanent physical and mental retardation, all of which are most probably caused by the hypercalcaemia. There was little evidence that prednisone, which was given for four months, produced any additional effect. The third hospital admission at 16 months of age was precipitated by hypoproteinaemia and hypochromic anaemia, both of which were undoubtedly caused by the diet which, as well as being low in calcium content, was too low in protein and iron. The low serum calcium noted at this time was probably related to the low serum proteins. When additional protein and iron were added to the diet, the serum proteins and haemoglobin returned to normal levels within a month.

Stapleton⁸ recently discussed the etiology of the disease and felt that a large intake of vitamin D was the main causative factor. E.E. received at most 1000 international units of vitamin D daily, which certainly could not be considered excessive, although an abnormal sensitivity to the vitamin might be an additional factor as suggested by Bonham Carter *et al.*⁹ Other authors,¹⁰ however, have observed no adverse effects from giving calciferol to patients with the disease. Forfar *et al.*¹⁰ suggested that an abnormal metabolism of cholesterol in these patients might produce a cholesterol derivative with hypercalcaemic and toxic effects. The serum cholesterol in E.E. was initially moderately elevated, as is usual in this disease.

Stapleton *et al.*⁸ also commented upon the curious geographical distribution of the disease, which has been much less common in North America than in Europe. They thought that a possible reason for this difference might lie in the claim that dried milk, which is mainly used for feeding infants in the United Kingdom, has a lower essential fatty acid content than evaporated milk, which is more commonly used in the United States. Deficiency of essential fatty acid may interfere with sterol metabolism and be followed by elevation of the serum cholesterol. Feeding a normal patient and a patient with idiopathic hypercalcaemia with cottonseed oil (rich in essential

fatty acids) resulted in a fall in the serum calcium in both cases. This attractive hypothesis was not confirmed in a later paper.¹¹ Others⁷ have suggested that the disease has been more common in the United Kingdom than in the United States because in the former milk preparations are, or were until recently, more heavily fortified with vitamin D. However, vitamin supplements are probably given more freely to babies in North America than in Europe. The dietary calcium intake must be a significant factor in the development of the disease, which has never been described in an exclusively breast-fed baby, cows' milk having about four times the calcium content of breast milk. It seems possible that the different feeding habits might be an explanation of the variation in incidence of the disease on the two continents. In North America it is common to begin mixed feeding at six weeks of age or even earlier, and by the age of three or four months, which is the usual age for the introduction of solids in west European countries, the American baby is getting a number of different solids and therefore drinks less milk. The earlier introduction of cereal, containing phytic acid which precipitates calcium in the gut as insoluble calcium phytate, would also reduce calcium absorption at a younger age. Cereal was first offered to E.E. when she was two months old, and the diet she received was no different from that of most babies on this continent. However, the well water used to dilute her milk was hard and contained 160 parts of calcium per million, i.e. 100 mg. calcium per pint of water. This is less than one-seventh the calcium content of cows' milk, but over a period of months the calcium absorbed from this source might be appreciable. Calcium absorption from the gut is influenced by many factors such as local pH and intake of vitamin D, phosphorus, fat and phytic acid, but, by and large, increased ingestion of calcium leads to increased absorption. It is interesting to speculate whether the high calcium content of the well water played any part in the development of hypercalcaemia in E.E.

SUMMARY

A case of the severe form of idiopathic hypercalcaemia of infancy is described.

Treatment with a low calcium diet was effective in lowering the serum calcium. Initial signs of renal insufficiency disappeared but the child was mentally and physically retarded when last seen at 22 months of age. Hypoproteinaemia and anaemia occurred because the patient's diet was low in protein and iron as well as low in calcium.

The reasons for the differing incidence of the disease in Europe and North America are discussed, and the variation in feeding habits on the two continents is considered as a possible cause.

I am grateful to Dr. Ethel McPhail of Boissevain, Manitoba, for referring this patient and for details about the early history. I also wish to thank Dr. M. McLandress and Dr. K. C. Finkel for reviewing the manuscript.

ADDENDUM

Since this paper was submitted for publication, Gibson¹² has described two mentally retarded adults at the Manitoba School, Portage la Prairie, whose mental defect seemed to have resulted from idiopathic infantile hypercalcaemia. These patients, both men, were aged 22 and 44 years, respectively, and in both there was an early history of vomiting and failure to thrive. They were dwarfed and mentally defective, showed some of the features of the "elfin" facies, had radiological areas of increased density in the skull and, most interesting of all, had elevation of the serum calcium. This is the first time that the condition has been described in adults.

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AN UNUSUAL SWELLING AT THE WRIST

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SWELLINGS about a joint are interesting diagnostic problems. They are commonly derived from synovial structures but may arise from any component of the joint or from overlying structures.

The following is the report of a swelling at the right wrist which was of muscular origin, the muscle being the palmaris longus.

The palmaris longus is a very interesting structure. It is absent in from 10 to 20% of people and is subject to numerous anomalies. It originates from the common flexor tendon which is attached to the medial epicondyle of the humerus and it also takes origin from the adjacent deep fascia. Classically it has a long tendon and is inserted into the palmar aponeurosis and into the transverse carpal ligament. In its action it is a feeble flexor of the metacarpophalangeal joint, wrist joint and the elbow joint. However, it may be muscular at the wrist joint and tendinous above, or it may have its muscle belly in the central portion and a tendon at either extremity. The following is the report of a case in which the muscle belly occurred at the wrist and increased in size because of hypertrophy, producing a swelling and discomfort.

A 26-year-old labourer was first seen with a two-year history of an increasing swelling over the volar surface of the right wrist. The swelling had first appeared some six months after he had begun weight-lifting (he is by trade a bricklayer). The swelling slowly increased in size and initially was not painful. During the last three or four months it had produced some discomfort while at work. For the last month and a half he had felt some paræsthesia over the lateral three digits. There was no history of trauma or tuberculosis. There were no symptoms referable to the left wrist. He was well nourished and well developed.

There was an ovoid swelling of the volar surface of the right wrist; this ended abruptly at the distal transverse crease of the wrist and extended proximally for some five to six cm. It was approximately 2.5 cm. wide. It felt quite firm, was not hard and there was no fluctuation. It was found to lie anterior to the flexor sheaths at this level, and on flexion of the wrist joint the swelling covered the flexor tendons centrally. The movements of the wrist joint were normal and the swelling did not extend into the palm. The circulation in the hand was normal, and the motor and sensory nerves were intact. There was some paræsthesia over the lateral three digits.

The swelling was explored through a transverse incision at the level of the proximal skin crease at the wrist. On arriving at the deep fascia of the forearm, a bluish swelling was noted and on incising the deep fascia the muscle was found to bulge into the wound. On examining the muscle it was found to be approximately 1½ in. (3.75 cm.) wide and approximately three-eighths of an inch (0.9 cm.) thick. It covered the flexor sheaths of the flexor digitorum sublimis and profundus. The tendons of the flexor carpi radialis and carpi ulnaris were lying in their respective positions and free from the muscle. The muscle was elevated and traced to the proximal border of the transverse carpal ligament; there it was found to end abruptly. There was no evidence of tendon, but numerous fibrous septa were found to leave the muscle to pass to the anterior surface of the ligament, and a few septa were also inserted into the proximal border of the ligament. The muscle was traced proximally for two inches (5 cm.) and it maintained its width and depth. In view of the bulk of the muscle and the patient's symptoms it was decided to partially excise the structure. Partial excision was chosen since complete excision might possibly have interfered with joint function. A triangular section of the muscle was therefore excised, leaving a width of three-eighths of an inch at the insertion and increasing widths as the structure was traced proximally. Hæmostasis was secured and the wound was closed in layers.

On final examination one month after the operation, function was found to be satisfactory.

SUMMARY

A case of swelling at the right wrist is discussed. The swelling was due to hypertrophy occurring in an anomalous palmaris longus muscle.

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Special Article

RESETTLEMENT CLINICS IN SASKATCHEWAN*

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INTRODUCTION

Resettlement Clinics in Great Britain

The term "resettlement clinics" may be as unfamiliar to many Canadians as it was to me a year ago. It may suggest such activities as settlement of veterans on the land. It was my privilege to spend six weeks in 1956 visiting various rehabilitation facilities in England, Scotland and Wales. While in Glasgow, I met Dr. Browning, a physical medicine specialist, who has had extensive experience running what he aptly calls "resettlement clinics." These were set up with the help of Dr. P. Ferguson, a professor of social medicine, in 1946, and are run periodically in connection with hospitals for various categories of cases, such as the tuberculous and the blind. The Glasgow area is divided into five regions of approximately 200,000 population each, and a resettlement clinic is associated with each region. For example, tuberculous cases from the Belvedere area are admitted to the Rob Royston Hospital Chest Unit. There is a standing arrangement by which all patients aged 16-30 are seen within one month of admission by Dr. Browning, with a view to planning their vocational rehabilitation at the outset of treatment. Selected cases in older patients are also studied. The conference which is called to advise on the rehabilitation of these patients includes the following: chest physician; health visitor (a public health nurse concerned with the home and hospital aspects of the case); hospital almoner (social worker); local disablement resettlement officer (D.R.O.); youth employment officer (concerned with employment of patients aged 16-18); group disablement resettlement officer (responsible for a group of employment exchanges which are equivalent to our unemployment insurance offices); Dr. Browning (acts as chairman of the conference in his capacity as medical consultant to the Department of Labour).

It is noteworthy that the entire group have the opportunity of interviewing the patient.

Comprehensive resettlement clinics have been operative for five or six years in Scotland and for a longer period in England. The inclusion of a group D.R.O. in the conference insures that work possibilities beyond the local area are considered for the individual case, and an additional feature instituted by Dr. Browning is a district co-ordinating service. The key man in this is the District Co-ordinator, who works in the same office

*Based on an address presented at the Fifth Annual Meeting of the Canadian Association of Physical Medicine and Rehabilitation, June 21, 1957.

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as the D.R.O. and follows up problem cases. This follow-up is facilitated by a Local Employment Exchange conference. The object of this is to bring some really high powered technical advice to bear on the patient's problems. The personnel of this conference are as follows: D.R.O.; industrial psychologist; technical officer of the Ministry of Labour (such as a consultant engineer); Dr. Browning; district co-ordinator (chairman).

Another technique is used for those patients whose problem is mainly one of social resettlement. For these, housing committee experts are invited to meet the representatives of the Department of Health and Welfare with Dr. Browning. Priority may be recommended in provision of new housing.

In addition to these activities, in most of which Dr. Browning has been a prime mover, his advice is available on request to local authorities with regard to medical aspects of housing, education and child care.

This excellent program meets most of the desiderata of rehabilitation in that patients are considered for rehabilitation early in the development of their disease process before they have become depressed, while those who have already become chronic cases are referred to the resettlement committees on the initiative of any of the medical or lay workers concerned. I have dealt with this matter at some length as it seems to me to approach more nearly the ideal than most other systems of which I am aware.

In Britain I also visited an industrial rehabilitation unit. This is a longer established and better known system in the rehabilitation process. These units are designed to prepare a man for work after he has finished his medical treatment. It is essentially a hardening up process in which both physically and mentally he becomes more work conscious. Resettlement clinics are also held in these centres, under the chairmanship of the lay manager.

At one that I attended the following were present: psychologist; vocational guidance adviser; D.R.O.; chief occupational officer (supervisor of work program at the I.R.U.); social worker; part-time general practitioner (oversees medical aspects of the unit); manager, non-medical (chairman).

The work was conducted speedily and efficiently so that 20 cases were studied in a morning.

During my tour I heard many comments on the role of the doctor in resettlement clinics, particularly in the I.R.U.s. These units are run by the Department of Labour, and the usual procedure is to employ a general practitioner part time. Historically, this work was begun by the Department of Labour at a stage when it seemed that the Department of Health was not ready to enter this field. Moreover, it was assumed that medical work would play a minor role in the centres because the patients were not supposed to be admitted to the centres until their medical treatment was completed. In actual fact it seems that one cannot really regard the patient's medical care as complete until he is fully established back at work. In the view of many well placed to pass judgment on this matter, it would seem better to have continuity of medical care by a specialist orientated

towards rehabilitation from start to finish of the patient's medical course. He would then be able to assess more readily the patient's physical and psychological responses to treatment, work-conditioning, training and employment, and would provide him with that regular reassurance and sense of security which are so essential to rehabilitation. In addition the patient needs strong support from others such as social workers, psychologists and placement personnel who can give guidance in their own special fields.

Unfortunately the location and organization of I.R.U.s and of the majority of other rehabilitation organizations are not compatible with this ideal of continuity of medical care. However, the difficulties experienced in the I.R.U.s would seem to be a strong argument for associating work-conditioning centres with rehabilitation centres where a specialist in rehabilitation work would be available.

RESETTLEMENT CLINICS IN THE UNITED STATES

In the summer of 1955 I had the opportunity of visiting the United States for seven weeks and of studying the rehabilitation organization in a Veterans Administration hospital. While there was the same type of approach, in that various different medical and lay specialists shared their experience in a conference on individual patients, the organization was simpler because practically all the personnel concerned were regularly in the hospital and could frequently have what we would call "curb stone" consultations. A point of interest was the alternating medical and lay chairmanship of these conferences.

RESETTLEMENT CLINICS IN SASKATCHEWAN

(a) *Department of Veterans Affairs*

The earliest comparable clinics in Saskatchewan, as in the rest of Canada, were those conducted by the Department of Veterans Affairs. The key men in this organization were the casualty rehabilitation officers. These were few in number and were faced with a staggering caseload at the end of the War. For example, in Regina there were only three such officers and they had an active caseload of 1100 in 1945. Nevertheless, within two years almost all the cases had been placed, thanks to good planning, close contact with employers and community interest in the veteran.

The initial approach was to allot 100 of the more difficult cases to each officer and to defer many of the less serious cases. It was found that, in fact, the large majority of the latter succeeded in re-establishing themselves without specific case work. Those selected for special help, usually including training, were the amputees, paraplegics and the blind. The system was that each casualty rehabilitation officer did what he could to advise and to place his active cases. Whenever he considered it necessary, he would obtain a specialist's advice or call a conference of interested personnel, but this was done in only a small proportion of cases. The work was carried out by the Welfare Services branch, and the onus was therefore upon the casualty rehabilitation officer to obtain what

ever medical advice and guidance was needed. From the administrative point of view it was considered by the national head of the Casualty Services branch that rehabilitation might have been facilitated by its being made a direct responsibility of the Treatment Services branch, under medical supervision. However, in spite of the enormous caseload and various administrative problems, the remarkable success achieved by the casualty rehabilitation officers is very greatly to their credit.

When it is recognized that very few of these officers were trained social workers and some of them had had no previous experience of selection for training or placement, their achievement is all the more creditable. It strongly suggests that a simple direct approach without an elaborate organizational structure can be brilliantly successful, provided there is good over-all direction and well-motivated personnel who are given the necessary facilities and freedom of action.

(b) *Department of Social Welfare and Rehabilitation*

Reference has been made previously (*Brit. J. Phys. Med.*, Jan. 1956) to the rehabilitation program of the Department of Social Welfare in Saskatchewan. This is a comprehensive vocational rehabilitation program designed for those handicapped persons who cannot be placed in employment without further training, but are likely to be good candidates for placement after an appropriate course of training either at a special school or on the job. In this program at the present time, there are three trained social workers, one in Regina, one in Saskatoon and one in North Battleford. These workers get to know the client very well and encourage him to make his own decisions about what he wants to do, and they maintain close contact throughout his rehabilitation. All cases undergo psychometric testing, and a comprehensive report is made by the family doctor. They are then referred with all available reports to one of us who are specializing in rehabilitation medicine. Following our study, additional investigations or consultations are arranged if necessary. In suitable cases the patient undergoes practical testing at a Vocational Rehabilitation Centre in Saskatoon, run by the Saskatchewan Council for Crippled Children and Adults. This vocational program is taken as far as possible to the patient's home community, as it is felt that in this way the services will be more acceptable to the patient. In addition, it helps to build up an interest in rehabilitation amongst the doctors, employment personnel and municipal officials.

At the present time Rehabilitation Assessment Conferences are held only in the three cities enumerated, but expansion to other cities is intended.

The principal conference members are as follows: supervisor of rehabilitation and disabled persons allowances (Department of Social Welfare); rehabilitation social worker; medical director, Physical Restoration Division, Public Health Department (as medical consultant to Social Welfare Department); psychologist; director of

guidance, Department of Education; special placement officer, National Employment Service; regional supervisor, Department of Social Welfare (chairman).

In Saskatoon and North Battleford, two vocational counsellors from the vocational rehabilitation centre carry out aptitude tests.

An invitation is extended to the family doctor and to specialists interested in the individual case. On appropriate occasions there may be a representative from a special agency concerned with the veteran, injured workman, farmer, Indian, deaf, blind or arthritic. Conferences are scheduled at four to six week intervals in each centre, three to eight cases being considered each time. Typed summaries are available of the reports from all who have studied the patient, and the recommendations of the conference are interpreted to the patient by his social worker.

(c) *Physical Restoration Division of Public Health Department*

In addition to collaborating in this program, we accept at a rehabilitation assessment clinic, held monthly at each of the Physical Restoration Centres in Regina and Saskatoon, out-patients referred by the Social Welfare Department with the agreement of the family doctor. In-patients are accepted for a similar purpose at the University Hospital. Many of these are applicants for disabled persons' allowance or for mother's allowance, and have been on social aid for years. If they are found to be fit or can be made fit for work, we urge them to seek suitable employment and we recommend that the financial support be cut at a time when work should be available. A few are recommended for vocational training under the Social Welfare Department, but most have been considered for this and rejected before we see them. Some suitable activity should be sought for such cases, and we therefore refer them for comprehensive studies similar to those given to the more promising cases by the Social Welfare Department. This usually entails residence for three days near the centre, and our social worker endeavours—with increasing success—to persuade the local municipality to underwrite maintenance and travel costs. Many cases benefit from therapy, bracing or surgery, and at least become more independent. Some engage in home-bound activities or are accepted in a sheltered workshop, while the occasional case is successfully restored to work. One such person was a 51-year-old Metis whose wife had been in receipt of mother's allowance for many years on account of his multiple disabilities. He had undergone an above-knee amputation on the right side at the age of 20. He was wearing a poorly fitting prosthesis, and had some sub-astragaloid and calcaneocuboid osteoarthritis in the opposite foot. There was some weakness from poliomyelitis involving both the right hip and the left foot, and he was subject to attacks of low back pain. On two occasions he had been sent on a course of barbering by the Social Welfare Department but had failed to complete the course. He stated that he would have worked as a barber had he not been afraid of getting into trouble with the law

if he started to do this without having the necessary certificate. A deadlock had been reached because he refused to take any more training as he considered his skill to be adequate. However, during a frank and private discussion he convinced me of his willingness to work. The representative of the National Employment Service informed us at the conference that it was not essential for a man to have a certificate before he started barbering. It was sufficient for him to commence doing this work and to report this to the Department of Labour; a representative of that department would, in due course, call upon him and see whether the standard of work which he was doing was adequate. This "back door" into barbering was news to the patient. Armed with this information he very shortly obtained a job, and a follow-up six months later showed that he had been in regular employment ever since. It seemed that in this case our interest in doing something to remedy his physical problems succeeded in gaining his confidence and that this led to his willingness to attempt work. The technical information provided by the National Employment Service representative showed the man how to get a start without losing face by changing his stand, and the interest expressed by the representative of the Social Welfare Department in following up his case contributed towards the successful outcome.

DISCUSSION

1. *Teamwork*

Not every case needs a conference, but when the problem is complex it should be studied in a comprehensive manner, from the medical, social, emotional, intellectual and vocational angles. This requires a minimum of three days, and may take many weeks. The patient must be taken into the confidence of his various advisers so that at all stages he remains in rapport with them. If this is done, there is frequently a marked improvement in his motivation as he recognizes that every one on the team is out to help him. When the team gets together to discuss his problems, it is essential that each member shall feel free to express his views candidly and even to question the opinion given by other members. Unless this atmosphere prevails, the group ceases to be a team and one or more members become undesirably dominant. I recall an occasion when I had to reverse my opinion on a matter which was clearly within my own special field, following a comment made by our social worker. The question was whether or not a young adult Indian should be persuaded to undergo surgery for a gross deformity of his hip. It was quite a surgical possibility to correct this, but the patient was loath to have it done. The social worker pointed out that the patient's unwillingness was based upon ignorance and that it would be wrong to allow him to refuse the great benefits of operation just for lack of orientation to hospitals and surgery. After she had shown him around the hospital and introduced him to a number of patients, he expressed his complete willingness to undergo surgery, which, he in fact did a few weeks later. In this question the social worker's judgment was better than my own.

This willingness to give and take, even in our own special fields, is the essence of team work. Whether a doctor is or is not chairman of a rehabilitation assessment conference is much less important than whether or not the chairman encourages this type of free exchange and exhibits a dogged determination to obtain the best possible deal for the patient.

2. *Exchange of Information*

There must be full exchange of all relevant data among government agencies such as Health and Welfare, Workmen's Compensation, D.V.A., Department of Indian Affairs, and voluntary health agencies. Unless this is done, needless difficulties are encountered.

Obsession with secrecy, far from benefiting the patient, may actually work against his best interests.

3. *Follow-Up*

One key person should carry out the follow-up. This may be a social worker, a placement officer of National Employment Service or Workmen's Compensation Board, a casualty rehabilitation officer under D.V.A., or a representative of some voluntary agency. It is not sufficient to advise the patient and let him go home without any follow-up. Unfortunately, at the present time, owing to lack of available personnel, it is rarely possible for us to obtain the necessary follow-up services after our resettlement clinics under the Physical Restoration Division.

4. *Patient's Attitude and Ours*

There is a strong tendency to take an adverse view of a patient who when first seen shows poor motivation or exaggerates symptoms. This fails to take into account the grave difficulties which the patient may have faced, and his natural fears that the doctor or rehabilitation workers may underestimate the severity of his condition. All concerned with rehabilitation should not consider the patient's attitude at the moment, but rather the attitude which may be engendered in him by strong reassurance, combined with active physical exercise in a rehabilitation setting. Whenever possible, these should be supplemented by carefully chosen, interesting and challenging work, preferably under male supervision. If possible, a poorly motivated patient should be allowed to exercise or work alongside a very well motivated patient in the hope that the latter will, by his example and vigorous encouragement, inspire better motivation. Other powerful motivating situations are camps and clubs for the handicapped.

5. *Financing*

There are certain basically financial problems which currently set a limit upon what can be done in rehabilitation. There is a shortage of social workers and National Employment Service officers and a dearth of funds which can be used for setting up a patient in his own business. There is virtually no money available which could be used to help a farm labourer, no longer able to do heavy work, to move from a rural to an urban setting with his family.

6. Community Participation

Responsibility should be more willingly assumed by communities. Local and regional rehabilitation committees should be formed with the object of rehabilitating their own disabled. It would be convenient to be able to refer cases to such committees, so that their extensive local knowledge would be available to help the patient.

7. Cooperation of Management

Personnel directors and other employer representatives should be invited to assist as members of resettlement clinics and of local and regional rehabilitation committees, especially when one of their own employees is involved. Larger firms could well copy the example of the Austin and Vauxhall motor factories in Britain by establishing a rehabilitation workshop for their convalescent employees.

8. Hospitals

Application of the resettlement clinic system to general and special hospitals should be encouraged. Development of departments of physical medicine under a trained specialist in physical medicine and rehabilitation and employment of medical social workers contribute much towards shortening the patient's stay in hospital. If such work is co-ordinated with that of vocational experts, his return to work is also expedited. The resultant saving of money by the family and by the community more than justifies the expense, while the contribution towards the happiness and security of patient and family is even more rewarding.

9. Special Centres

The proven value of special centres for rehabilitation of the injured workman is well known in Canada, although this knowledge is not yet being applied by every provincial Workmen's Compensation Board. In the U.S.A., the Liberty Mutual Insurance Company has similarly demonstrated, at its Boston and Chicago centres, not only the economic value to the insurer but the many gains to the insured.

Sheltered Workshops for the physically handicapped, the blind, deaf, tuberculous, and mentally retarded should be carefully considered, but only for those whose disability prevents their employment in the open market. A reasonable living may also be made by some in a homebound program.

An adequate Resettlement Clinic will use all facilities and help to draw the attention of community leaders to needs which are not yet being met.

10. Prevention of Neurosis

When a patient is faced with the possibility of a permanent disability, it is of fundamental importance to forestall the onset of depression, anxiety, hysteria, malingering, and disabling psychosomatic symptoms. The most certain way to achieve this goal is to have an early frank, but optimistic talk with him about the true nature, extent and probable outcome of his injury or illness. This was impressed upon me during a

two-year period spent as assistant surgeon at the Birmingham Accident Hospital and Rehabilitation Centre in England, followed by a year spent as a surgical consultant with the Workmen's Compensation Board of Ontario. Illustrative cases were subsequently published (*Ontario Medical Review*, August 1952).

Unfortunately, it is still true that many a patient with coronary thrombosis, pulmonary tuberculosis, back or head injury, poliomyelitis, or paraplegia needlessly enters the ranks of the unemployed or the "chronic sick" for lack of well-informed and sympathetic but firm guidance along the road to rehabilitation by his attending doctor. All too often, no skilled prognostic study is made or vocational advice given until psychological breakdown is almost irreversible. At this stage, the doctor often supports the patient's request for permanent financial support from the State. Alternatively, he may try to force the patient back to work with the statement that there is nothing wrong with him. In the former case the independence of the home and the self-respect of a human being have been undermined. In the latter case, a long and bitter strife begins between an aggrieved patient and an adamant government or insurance agency. The intractability of this situation is so notorious that prevention is the obvious solution.

SUMMARY

A realistic vocational goal should be established within the shortest possible time after a patient develops an illness or suffers an accident which may interfere with his return to his previous occupation.

Vocational studies may be carried out in hospital, home or special centre, and the attending doctor should be familiar with and fully utilize the community resources, medical and lay, and endeavour to secure their expansion where necessary, so that no patient is needlessly idle.

Examples are given of successful resettlement clinics in Britain, Canada and the United States, and criteria for success are outlined.

OF NO PRACTICAL IMPORTANCE

"One day this spring while I was riding from the first floor to the sixth, the elevator was invaded at the second floor by one of our clinical instructors and his entourage of four or five senior medical students. I paid little attention to their conversation until I heard one of the students voice an old and all too familiar refrain. 'But, Doctor,' he said, 'since it has no practical importance, why should we waste time on that?'"

"I do not know whether the statement of the student was in reference to a recent examination, to a patient he had just seen, or to some academic feature of a medical problem; but I was full of sympathy for the clinical instructor who, as the elevator door closed behind them, was beginning his explanation of why he felt a physician should be concerned with many things in medicine other than those which are strictly practical.

"The response of this student revealed little evidence of an enquiring mind, and, therefore, a shocking lack of intellectual development. A senior medical student certainly should realize that if physicians concern themselves solely with that which is practical or useful, all progress in medicine will soon cease."—*Quart. Bull. Northwest. U. Med. School*, 32: 303, 1958.

SHORT COMMUNICATION

OUTCOME OF NINETY CASES SIMULATING PLACENTA PRÆVIA

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THE OUTCOME of placenta prævia is well known, and has been adequately described elsewhere.¹⁻⁴ The outcome of cases involved in the differential diagnosis of placenta prævia is not so well documented, however, and is the subject of this article.

Placenta prævia should be suspected in the presence of antepartum hæmorrhage or a persistently unstable presentation of the fetus. During a recent evaluation⁴ of radiological diagnosis of placenta prævia, 107 suspected cases were investigated at the Leicester General Hospital, England. Placenta prævia was demonstrated radiologically and confirmed clinically in 14 cases. In three other clinically proven cases the radiological examination was in error in one case and unsatisfactory in two cases. In the remaining 90, placenta prævia was excluded radiologically and clinically.

ANALYSES

The distribution of all cases is shown in Table I. Group A consists of cases of proven placenta prævia. Group B contains the cases which simulated placenta prævia.

TABLE I.—DISTRIBUTION OF 107 SUSPECTED CASES OF PLACENTA PRÆVIA

Placental site	Total cases	Presenting as antepartum hæmorrhage	Presenting as unstable lie
<i>Group A</i>			
Placenta prævia confirmed.....	17	15	2
<i>Group B</i>			
Placenta prævia excluded.....	90	54	36

TABLE II.—CAUSES OF ANTEPARTUM HÆMORRHAGE IN GROUP B

Placenta	Cervix	Undetermined
Abruptio..... 16	Erosion..... 2	No cause found..... 30
Circumvallata 3	Varicosities... 1	
	Polyp..... 1	
	Carcinoma.... 1	
Total cases... 19	5	30

TABLE III.—METHOD OF DELIVERY IN CASES OF UNSTABLE LIE IN GROUP B

Delivery via	Total cases	Surgical induction of labour	Spontaneous onset of labour
Vagina..... 26		8	18
<i>Reasons for Cæsarean section</i>			
		Failed trial labour	Deteriorating toxæmia
		Fibroid in lower segment	Obstruction from ovarian dermoid
Cæsarean section.... 10	7	1	1

TABLE IV.—WEIGHTS OF INFANTS IN CASES OF UNSTABLE LIE IN GROUP B

Weights	Under 7 lb.	7 to 8 lb.	8 to 10 lb.
Cases.....	10	12	14

TABLE V.—RADIOGRAPHIC LOCATION OF PLACENTA IN GROUP B

Placenta in upper uterine segment	Not encroaching on fundus		Encroaching on fundus		Total cases
	Antepartum hæmorrhage	Unstable lie	Antepartum hæmorrhage	Unstable lie	
Anterior.....	30	19	3	4	56
Posterior.....	13	8	8	5	34

Factors relating to Group B cases are shown in Tables II, III, IV and V. These factors include the causes of antepartum hæmorrhage, methods of delivery, infant weights, and the site of the placenta in the upper uterine segment.

SUMMARY

The outcome of 90 cases simulating placenta prævia is analyzed. The location of the placental site is given.

One group of cases presented as antepartum hæmorrhage. The causes of bleeding are tabulated.

A second group of cases presented as a persistent unstable lie in the absence of antepartum hæmorrhage. The method of delivery and the weights of the infants are shown.

I wish to thank Mr. D. R. Cairns, Consultant Gynaecologist, and Dr. J. L. Freer, Consultant Radiologist, for their assistance and helpful criticism during the investigation at the Leicester General Hospital.

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ANXIETY IN PARENTS

"Current psychiatric teaching has, I believe, only increased parental anxiety, shaken faith in their own ability to rear children and undermined parental authority. That every act of the parents as it concerns the child has permanent meaning; that a frustration is harmful; or that the child development process is hazardous or delicately balanced, is only a psychiatric fallacy. In America the influence of these false teachings is widespread. Pleasures of parenthood are tempered by anxieties, uncertainties and feelings of inadequacy and guilt. I am all too frequently asked—'I did so-and-so to my child. Did I make a mistake?' It is not surprising that parents unsure of themselves and their behaviour are unable to exert direction and authority which the child expects and needs for his development. Children sense this parental anxiety and unsureness and take on these feelings themselves. Concentration on parental affection has led to fear that discipline will jeopardize parent-child relations."—E. A. Wishrope: *Harper Hosp. Bull.*, 16: 197, 1958.

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(Information regarding contributions and advertising will be found on the second page following the reading material.)

THE STUDY OF MORBIDITY

The difficulties besetting mortality statistics, due to inadequate recording of death certificates, are quite insignificant when compared with those related to morbidity statistics. At best, our knowledge with regard to the incidence of diseases, particularly those that are non-fatal or chronic, is an educated guess. Even in such diseases as diabetes, hypertension and heart disease, and cancer the morbidity rate is based on estimates and on sample studies. Reference to several studies of groups of general practices, an internist's practice and a sample study of an insured population was made in a paper dealing with an internist's personal experience.¹ Hans Pacy has recently reported his findings in a small country practice in Australia over a period of three years.² The reasons he advances for the need for morbidity studies are that they would serve as an important guide to the pharmaceutical industry, to charitable organizations, and to medical schools. He quotes Henry Shannon as saying in 1957 that we are sadly in need of a *bill of morbidity*.

The ideal morbidity recording should, according to Pacy, embrace the entire population continuously. The details should be kept simple, and diagnoses should be accurate and internationally comparable. He suggests that a system of comprehensive recording could be introduced in three stages, namely, a diagnostic stage, a therapeutic stage and a stage of complete medical audit. The latter would include estimation of loss of wages, costs of benefits and drugs, and medical and hospital bills. The difficulty of achieving even the first stage—the recording on cards or in a book of personal data regarding each patient; an accurate diagnosis and an indication of chronicity or otherwise—is to be overcome by paying doctors a small fee for each entry. Regional morbidity committees should supervise, develop and study the recording methods and adjust them with the help and advice of representatives of the Registrar-General's Department.

The next two stages would be introduced after successful operation of the first stage, depending of course on the availability of finance for this purpose. In order to demonstrate the feasibility of the first stage of recording, Pacy presents his own records of morbidity. The analysis of these records enables us to form a fairly true picture of the type of practice Pacy has, the composition of its population, the most common conditions which he had to deal with, and the proportion of cases in various specialties which he encountered. It could well serve as a guide for teachers of medical schools if they were able to consult similar tables compiled in various parts of many countries. It may be argued that the number involved in this study is too small to draw any conclusions from it. This may be true as regards the application of the findings of this morbidity study to other areas. But the importance of this study, and of the few similar studies carried out by single doctors without the help of the statistical machinery of health departments, lies in the spirit behind it. What was done by Pacy can be done by others, and if enough such reports accumulate we shall have a better knowledge of morbidity, and a truer perspective about the relative incidence of diseases encountered in general practice and in hospital practice.

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Editorial Comments

TIMED-RELEASE PREPARATIONS FOR ORAL MEDICATION

There are obvious advantages to the physician in being able to prescribe a preparation which in one dose contains sufficient medication to last all day or all night. It is natural, therefore, that the pharmaceutical industry has sought to incorporate a variety of drugs into prolonged, sustained, delayed, repeat action or other timed-release preparations. Advertisements describe, often in very specific terms, just when and how much of a drug is released, and simplified curves of blood levels or clinical response depict how the preparation will act. The physician might obtain the impression that these preparations are easily standardized and that they behave exactly as advertised. Relatively few published data are available to support this impression.

The widespread use of these preparations has been a source of considerable concern to several groups, including the Council on Drugs of the American Medical Association, who have authorized a report by Dr. Carl A. Dragstedt¹ on the subject. Referring to work carried out at the Food and Drug Laboratories in Canada,^{2,3} he concluded that "a preparation which actually succeeds in delaying the disintegration of the ad-

ministered form, and thereby the absorption of the active ingredient to any dependable degree, inevitably does so at the expense of some loss in precision of dosage". This would imply that it may be impossible to manufacture a prolonged-action product which will release essentially all its dose to the body. While the precision of dosage of many prolonged-action products on the market may be questioned, recent unpublished data would suggest that it has not been sacrificed in *all* such products. Since our early work has been the basis of Dr. Dragstedt's comments, it may be of interest to review the situation, particularly in the light of these more recent data.

There is no doubt whatsoever that more attention should be given to precision of dosage in timed-release medication. Calculation of the percentage of drug dose excreted in the urine in relation to that excreted from a standard preparation provides information on the physiological availability of the drug, and may be considered as a quantitative method of measuring precision of dosage. Early work³ demonstrated that ordinary coated tablets which did not disintegrate in one hour by an *in vitro* test were not physiologically available to human subjects, as judged by excretion of riboflavin and sodium p-aminosalicylate. Since the *in vitro* disintegration times of most of the 12 timed-release tablets investigated were much longer than this, it was suggested that their ingredients might not be fully available to the consumer. Obviously, the precision of dosage of drugs in these preparations would be of a relatively low order. On the other hand, the data also implied that timed-release products which disintegrated in about one hour or less would be fully available and that, in such products, absorption of the drug by the body may be prolonged or delayed but not reduced, thereby producing the desired effect with no loss in precision of dose. Preliminary observations suggest that this is true, for there are on the market some effective timed-release and enteric-coated tablets which disintegrate in less than one hour *in vitro* and which are fully available. Incidentally, it should be pointed out that *in vitro* disintegration times are not identical with *in vivo* release times, as has been implied in some of the literature.

Amphetamine is probably more widely incorporated into sustained-release preparations than any other drug. Data now being accumulated on urinary excretion rates following doses of amphetamine in this form indicate that there are marked differences between apparently similar products. Preparations labelled as containing 15 mg. amphetamine in sustained-release form have been found to yield from 5 mg. of drug available over a 24-hour period to 15 mg. available at once. Most subjects could detect no effect from the former but received a marked "jolt" from the latter. Only two of eight pellet preparations examined exhibited sustained release at an adequate level. Since there is no evidence to show that the situation is greatly different with other drugs in this form, it would appear that there may be many such products on the market which do not have the precision of dosage desired. As pointed out by Dragstedt, there is cause for concern about their use. The data also demonstrate, however, that

contrary to Dragstedt's feeling, sustained-release products if properly formulated can furnish precise doses which are fully available. Such characteristics, in both the tablet and pellet form, appear to lie in a relatively narrow area between a lack of sustained effect on one hand and low availability on the other. Relatively few manufacturers seem, as yet, to be able to define this area satisfactorily.

Dragstedt concluded his review with the statement, "The cautious physician would be wise not to become unwarrantedly optimistic as to the precision with which the prolonged type preparation can achieve the theoretical goals envisioned for them." There are very good reasons for this cautious view until further data are obtained. Uniform methods for the evaluation of these preparations are not yet available. *In vitro* methods which are widely used are meaningless unless they have been standardized by comparison against quantitative *in vivo* procedures. *In vivo* procedures, including clinical response, must be quantitative, objective and adequately controlled. Where adequate procedures have been used, very marked differences have been observed between products labelled as being similar. In addition to quantitative clinical data, there is an urgent need for more fundamental information on the absorption, distribution, and excretion kinetics of all drugs which are administered in timed-release forms. The importance of such information has been clearly indicated in the work of Swintosky *et al.*⁴ and Nelson.⁵

J. A. CAMPBELL

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TOPICAL STEROIDS—A SECOND LOOK

This subject was surveyed in these columns about three years ago.¹ Topical steroids continue to be widely used. Some common indications are localized atopic dermatitis, allergic contact dermatitis, primary irritant dermatitis, peri-anal and perivulvar dermatitis, and intertriginous psoriasis. Topical steroids have no effect on poison ivy dermatitis.^{2,3} It is important to choose the base appropriate to the stage of the eruption and the area involved (greasy bases should not be applied to either hairy areas or acute weeping dermatoses; very light vanishing-cream type bases are not always suitable to dry scaly eruptions). Occasionally a sensitivity to the vehicle will cause a contact dermatitis. Such a case is reported by Sams and Smith.⁴ The following strengths are adequate in most cases: 1/2% hydrocortisone, 1/10% fludrocortisone, 1/2% prednisolone, 1/10% triamcinolone. Schamberg *et al.*⁵ report no significant difference in 217 patients between the effect of 0.1% fludrocortisone lotion and 1.0% hydrocortisone lotion, or in 116 patients between 1.0% hydrocortisone lotion and 1.0% prednisolone lotion. These findings con-

firm the writer's impression that if an eruption does not respond to 1/2% hydrocortisone it will not respond to any topical steroid; in most of these cases the failure is due to a wrong diagnosis, or failure to remove etiological contact or irritant factors. This emphasizes the need to make an accurate pre-treatment diagnosis and not to forget other standard dermatological therapy. A contact dermatitis of the eyelids from nail polish will not be cured until the patient stops wearing the nail polish.

The possibility that topical steroids are being over-used is raised by two recent publications. Haxthausen⁶ reported on patients with allergic contact dermatitis in whom he produced eczematous reactions on four symmetrical sites by application of four 2 sq. cm. patch tests. One site was treated daily with 1% hydrocortisone, one with pure ointment base and one with coal tar, and one was left untreated. No significant difference was found between the areas treated with the three different ointments and the control site. He concludes that the favourable effect seen following the use of tar or hydrocortisone ointment depends probably "on other processes than an effect on the acute eczematous reaction itself". Schamberg⁵ and his co-workers report that in 177 patients in whom 0.1% fludrocortisone lotion was compared with control lotion base, no statistically significant difference in effect could be demonstrated. They discuss possible explanations including placebo effects and psychosomatic factors. It should be noted that some of the diagnoses listed are conditions not usually responsive to topical steroids (e.g. miliaria, psoriasis, intertriginous moniliasis). Perhaps a more critical selection of test cases would have shown evidence of the effectiveness of topical steroids.

Meanwhile the diarrhoea of advertising, samples and new names continues unabated. The comments of John Lear,⁷ Science Editor of the *Saturday Review*, apropos of the Madison Avenue type of advertising used to sell drugs, surely are applicable to topical steroids. In addition to the gross lack of informative advertising is the fact that many of the multiple kickapoo-juice type preparations have no place in the medical treatment of skin diseases. Also, the addition of many ingredients raises the price. Only two basic prescriptions are required: one is topical steroid in a lotion or light vanishing-cream type base (e.g. 1/2% hydrocortisone free alcohol in Dermabase), and the other is a topical steroid in a cold-cream type base (e.g. 1/2% hydrocortisone in Eucerine 60%, water 40%). If the physician will take the time to write his own prescriptions he will save his patients much money. (In Ottawa, 15.0 g. of either of the above prescriptions retails for about \$2.50; 5.0 g. of comparable ready-made preparations costs about \$1.85.) Only rarely is it necessary to incorporate other agents with the topical steroids. Vioform, 1%, may be used in combination when necessary.

In summary: (1) as with all intelligent medical therapy, a diagnosis is essential; (2) in many conditions the action of topical steroids is only repressive, not curative; (3) attention to the usual dermatological therapy is required; (4) the type of vehicle must be appropriate to the stage and

location of the dermatitis; and (5) for most conditions a 1/2% strength hydrocortisone is adequate.

ROBERT JACKSON

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POLITICS AND ATHEROMA

The intrusion of politics into science has rarely been helpful to the latter, or of value in clarifying obscure issues. It is therefore unfortunate that the cold war has now been carried into the already confused field of atheroma, as exemplified by a publication by a Russian internist.

This is all the more unfortunate since in a recent editorial in the *Annals of Internal Medicine* (49: 699, 1958), Dock paid a tribute to the Russian scientists who, starting with Ignatovski 50 years ago, were the first to produce severe arteriosclerosis in rabbits by feeding them milk and egg yolk. Dock provides a comprehensive review of the history of 50 years of experimental, clinical and population studies in arteriosclerosis. He regards it as established that coronary artery disease can be caused by diet, and cites as his most convincing proof the fact that 50% of the American dead in the Korean War, whose average age was 22 years, showed grossly visible atheromata, and that in 10% one coronary artery had its lumen reduced more than 50% by these lesions. The Korean and Chinese soldiers, whose intake of milk products is negligible and whose consumption of eggs and meat fat is low, showed no atheromata in their coronary arteries. Dock compares the present-day resistance to the acceptance of this relation of diet to coronary disease to the resistance in the past to other epoch-making discoveries, such as the role of bacteria in disease.

The emphasis on socio-economic stress and heredity reminds him of the importance attributed to them in the etiology of phthisis before the discovery of the tubercle bacillus and for some time afterwards. Stress has been shown to raise blood cholesterol levels but, as Dock points out, the exposure of Koreans and Chinese to 20 years of war and revolution did not produce the widespread atheromatosis in their 20-year-old population which was found in American youths, who hardly knew the meaning of socio-economic stress.

A conference on atherosclerosis and coronary artery disease in Soviet Russia was referred to in these pages some time ago (*Canad. M. A. J.*, 79: 1007, 1958). At this, Anichkov and his group pressed their conviction that atherosclerosis is a potentially reversible process and not an inevitable outcome of aging. It is of interest that Anichkov, a pupil of Ignatovski, published his first results in experimental atherosclerosis in 1914, and Dock rightly considers his research in this field as one

of the most original in the history of science. Ignatovski is believed to have had the idea for this work from observing the difference in diet and in severity of arterial lesions in the rich and poor, the milk-drinking tribes and the grain-eating and vegetable-eating peasants.

While still under the impression of Dock's glowing tribute to Russian scientists in general and their medical research workers in particular, we were surprised to read an article by a Soviet internist, Gurevitch, which differs in many respects from the foregoing. Gurevitch reviews the writings of workers in Western countries on the rising incidence of coronary artery disease and shows that he is well informed on this subject (*Klinicheskaya Med.*, 8: 17, 1958). He disputes the conclusions drawn by writers in the Western countries that a high-fat diet is related to coronary disease, and is particularly critical of the social-pathology studies in capitalist countries. In these, evidence is presented that the incidence of coronary artery disease is much higher in the professional classes than at the other extreme of the social level. He ignores the conclusions from studies (which he mentions) that exercise, at least of a moderate kind, seems to have a protective effect on the coronary arteries.

The statistics on the relationship between low-fat and low-calorie diet and infrequency of myocardial infarction in some primitive tribes are dismissed as not reliable because of insufficient diagnostic accuracy and paucity of local medical personnel. He is convinced that the increase of coronary disease in capitalist countries during the last 30 years is due in the main to the strain and stress of two World Wars and of modern life, and to the lowering of the standard of living of the toiling masses. He is particularly critical of the suggestion put forward by Western medical writers that fat intake should be restricted in order to reduce the incidence of coronary artery disease. This suggestion, he says in righteous indignation, "is advantageous to the ruling capitalist classes who are at present engaged in lowering the living standard of the masses, in lowering their wages and in raising the price of food and particularly of fat. The masses in capitalist countries suffer from a shortage and not from an excess of fat."

Our own experience does not bear out the contentions of Professor Gurevitch. In 1938, the depression in Newfoundland was at its height and tuberculosis morbidity and mortality were very high. In that year and in the following five years of practice in a fishing and farming community we saw only one case of death from myocardial infarction, and that in a man of 70. Angina pectoris was also rare. With improvement of living standards in Newfoundland after World War II, myocardial infarction became increasingly common whilst tuberculosis incidence was sharply reduced. Although no breakdown of the incidence of myocardial infarction by social class is available for the whole island, it has never been suggested by any of the medical practitioners that physical work and poor diet were responsible for this change, but rather the reverse.

Critics of any prevalent theory in science deserve to be heard, and re-examination of statistical evidence is welcome—particularly when it comes from scientists whose upbringing and outlook are so vastly different from our own. What one finds impossible to accept, however, is the suggestion that Western bourgeois scientists are politically prejudiced in their studies of coronary artery disease. These, according to Gurevitch, are an attempt to gloss over the actual social factors underlying the increase in coronary disease. Perhaps his viewpoint is the result of prolonged indoctrination by a system which had to justify its demands on its own workers by telling them that workers in capitalist countries are even worse off. Without wanting to appear self-righteous, we submit that medical scientists of the Western world have in a large measure been able to avoid being influenced by politics.

Much as this standpoint of our Soviet colleague may be regretted, it is important for us to know that such views are being expressed in other parts of the world, and that our interpretation of facts and figures is not the only one possible. The gulf between East and West will be bridged only if we are made aware of the thinking of our counterparts on the other side of the Iron Curtain and if we are able to transmit our thinking to them by direct contact.

W. GROBIN

CLINICAL CONSIDERATIONS IN MITRAL VALVULOPLASTY

During the past ten years surgical operations on the mitral valve have become reasonably commonplace, and a great mass of data has been accumulated with regard to this procedure, its indications, its limitations and its results. This information has been collected in the most rapid fashion possible by the use of haemodynamic and other similar quantitative measurements. Such an approach was urgently necessary in order to provide the greatest possible amount of information in the shortest possible time, and thereby arrive at a decision whether or not mitral commissurotomy should be retained as a therapeutic procedure.

The fundamental question, "Does mitral valvuloplasty prolong life in patients with mitral stenosis?" has not yet been answered, and will not be answerable for some years to come. However, it is now becoming increasingly clear that, except in unusual cases, complex haemodynamic studies are not required to determine operability, or to decide on the presence or absence of indications for surgery, in pure mitral stenosis. In a recent clinical review of the subject, Riss and Levine^{1, 2} argue from this, that, given facilities for accurate clinical diagnosis, reasonably adequate surgical equipment and well-trained surgical teams, the procedure of mitral commissurotomy need no longer be restricted to the largest medical centres. It would also appear to these observers that the reservoir of patients with operable mitral stenosis is sufficiently large to occupy the attention of a large number of

surgeons in larger and smaller centres throughout Canada and the U.S.A., for several years to come.

With this concept in mind they have analyzed their clinical data on 72 personally treated patients who had 74 operations for mitral stenosis. Their intention is to provide a series of clinical criteria as a basis for a decision on severity of disease, operability and postoperative prognosis; it is their thesis that this decision can be made on purely clinical grounds.

They first emphasize that, although the surgical mortality in this series was 8%, the latter portion of the study (two to three years) has been carried out with a surgical mortality of only 1%, even in patients with moderately severe symptoms. Furthermore, they point out that, of the 58 patients who recovered from the surgical procedure and could be followed up, only 8 were either unchanged or worse after surgery, while 50 showed varying degrees of improvement, mostly of a rather high degree. It is clear, therefore, that surgery for mitral stenosis can be performed with a decreasing operative risk, comparable to that of major abdominal surgery; that results are, on the whole, satisfactory; that improvement is to be expected in the majority of cases; and that this improvement can be maintained for some years.

Certain extremely interesting correlations emerge from this meticulously conducted study. For example, it was found, in line with previous suggestions, that there is a relative antagonism between very tight mitral stenosis and marked hypertension. This finding appeared valid when approached from either direction. When hypertension was present, there were no tight valves; and in cases of tight or very tight mitral stenosis there were few hypertensives.

It is of some interest to dwell on the effect of mitral commissurotomy on the auscultatory findings. Although, in many cases, very little change can be demonstrated in these findings after operation, certain trends can be recognized. For example, in approximately half the cases there was a decrease in the intensity of the mitral diastolic murmur. As to the systolic murmurs, the picture is not so clear. Some of these are undoubtedly due to associated mitral insufficiency, and the intensity of these may increase after valvuloplasty, because regurgitation is increased by the surgical procedure. Others may not be mitral in origin at all, but may represent functional tricuspid insufficiency with the systolic murmur transmitted to the left; and these may be expected to decrease in intensity or even to disappear after successful valvulotomy. However, according to the authors, a systolic murmur of moderate intensity or louder is occasionally found where the mitral valve is considerably stenosed and regurgitation is either absent or minor. Although they propose various explanations for this finding, and consider it "puzzling", this writer is of the opinion that most if not all of these are due to functional tricuspid insufficiency.

Another point in assessment of operability for mitral stenosis is determination of the origin of a basal diastolic murmur. These murmurs are, of course, the result of either pulmonic or aortic insufficiency. The former is of no significance and

will almost certainly disappear after a successful valvulotomy, while the latter may even contraindicate such a procedure. Most commonly, recourse to electrocardiography and fluoroscopy to assess the size of the left ventricle will settle this problem, if indeed it cannot be clarified by the search for the peripheral signs of aortic insufficiency.

Calcification of the mitral valve appears to present a somewhat greater immediate operative risk and a slightly less favourable final outcome.

It is well known that a large proportion of patients with mitral stenosis have associated atrial fibrillation; the authors are unable to state whether or not this arrhythmia has a deleterious effect on the final outcome of valvulotomy, except when it represents a late stage in the natural history of the disease. They are able to draw some conclusions, however, as to whether or not attempts at conversion should be made. In general, it would appear that "fixed" atrial fibrillation is best left alone both before and after operation while fibrillation precipitated by surgery should be treated by quinidine postoperatively.

Despite earlier suggestions to the contrary, the clinical analysis in this group of patients reveals that results of valvulotomy are quite satisfactory in patients who have had attacks of pulmonary oedema or hæmoptysis, or both. It has been known for some time that attacks of acute pulmonary oedema in atrial fibrillation are not so ominous as similar episodes in hypertension, aortic valve disease or coronary artery disease; similarly, attacks of hæmoptysis in mitral stenosis, representing as they do a safety-valve mechanism, are of less serious import than in other diseases.

The authors make interesting observations regarding peripheral embolism in this disease. For the past few years it has been emphasized that mitral surgery sharply decreases the incidence of cerebral embolism during subsequent years. So completely has this concept been accepted that in many centres peripheral embolism is considered to be an indication for valvulotomy in mitral stenosis, even in the absence of other indications. The authors make the point, however, that in the natural history of the disease, without operation, the frequency of peripheral embolism decreases in any case; and they suggest that the decrease in this complication after surgery may be more apparent than real. They also emphasize the rather obvious point that congestive heart failure is an indication for commissurotomy rather than a contraindication to it, provided that it is adequately treated medically before operation.

Contrary to popular opinion, there is very little relation between preoperative electrocardiographic findings and ultimate clinical improvement. In the experience of most observers, the value of the electrocardiogram lies in its ability to provide a rather rough guide to the presence of either right or left ventricular hypertrophy and thereby cast suspicion on the presence of a concomitant mitral regurgitation or aortic valve disease.

The prognostic value of x-rays is also very limited with respect to expected results of surgery. If one uses the term "x-ray" to indicate a six-foot

postero-anterior chest roentgenogram, as distinct from detailed cardiac fluoroscopy, one finds that it is of little help, even with respect to gross increases in total heart size. The largest hearts are those with complicating valvular lesions such as mitral insufficiency or aortic valve disease, and these are usually excluded from calculations of operability early in the clinical investigation. In uncomplicated mitral stenosis, the heart is apt to be surprisingly small and the typical configuration is so familiar that it does not merit further discussion here.

It is of great interest, and a source of gratification, to be able to state that age is only a slight factor in the outcome of surgery, and that satisfactory results are common in patients over 50 years of age. It is quite clear that, within reasonable limits, the decision to operate must be made on the basis of criteria other than age.

As might be expected, the preoperative degree of stenosis has a very important bearing on the final outcome. It should be obvious, and this was borne out by the analysis of results, that the tighter the stenosis (i.e., the smaller the size of the valve orifice) the better the results. Other things being equal, the average degree of improvement in cases with tight mitral stenosis in this series was twice that obtained in patients with moderate valvular narrowing.

This study is a most valuable one, chiefly because it demonstrates the tremendous volume of information that can be derived from a careful analysis of purely clinical data. In an era in which papers on cardiology are becoming more and more oriented in the direction of pure physiology and electronic engineering, this emphasis on clinical information is most refreshing.

S. J. SHANE

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"MAPLE SYRUP URINE DISEASE"*

Two cases of the rare disorder, "maple syrup urine disease", first described in the U.S.A., are reported in the January 10, 1959, issue of the *British Medical Journal* (pp. 90 and 91).

Mackenzie and Woolf describe a case in a 4-month-old girl who was studied at the Hospital for Sick Children, London. This child was severely mentally deficient, and was jerking her limbs and becoming cyanosed and breathless. A fresh specimen of urine had an odour very similar to that of maple syrup. The urine was free of protein but contained large amounts of valine, leucine and isoleucine. The "maple syrup" smell was due mostly to alpha-hydroxy-acids and to keto-acids present in the urine in large amounts.

The fasting blood sugar level was 52 mg., and after a feed only 60 mg. per 100 ml. It is suggested that amino acid metabolism is blocked (possibly through inborn absence of an enzyme) and that as in phenylketonuria the abnormal metabolites and/or amino acid concentration causes the cerebral dysfunction. A diet low in valine, leucine and isoleucine is thought to be worth trying in this case, as low phenylalanine diets have produced some improvement in phenylketonuria.

The prognosis is considered worse than in the latter condition, as can be seen from the second case, reported by Dancis *et al.* In this obviously retarded child, who died at the age of 20 months, maple syrup urine disease was discovered at the age of 4 months. Essentially, the laboratory findings were the same as in the first case.

Clinically, there is a similarity with phenylketonuria, for which this condition can be easily mistaken. The smell of the urine can be missed unless one is on the lookout for it. Amino-acid chromatography differentiates the two conditions conclusively, but it is worth while remembering the similarity and trying to elicit the maple syrup smell by acidifying the urine with dilute sulfuric acid.

W.G.

WILL YOU BE DRIVING IN EUROPE?

Many members attending the conjoint B.M.A.-C.M.A. meeting in Edinburgh have arranged to hire a self-drive car for their touring before and after the meeting. We have been advised by the Automobile Association of Great Britain, through its affiliate the Canadian Automobile Association, that such members will avoid trouble in establishing their right to drive by taking with them a valid 1959 driving licence issued by the Canadian province in which they reside.

So, if you have arranged for a car in advance or plan to hire one after arrival in the United Kingdom, do not forget to take your driving licence.

If you plan to travel by car on the Continent, you are reminded that Austria, Spain, Portugal and Yugoslavia require an International Driver's Licence. For Germany you require to have a German translation of your Canadian driver's licence. Aid and information on both of these matters may be obtained from your provincial Automobile Club or League or the Canadian Automobile Association, 6 Adelaide St. East, Toronto 1.

Our official travel agents, University Tours Ltd., 2 College Street, Toronto, have negotiated a very favourable accident insurance policy. Any member, whether he is utilizing the facilities of University Tours or not, may cover himself for motor travel in Europe.

*See also Letter to the Editor, page 483.

Medical News in brief

ACUTE PANCREATITIS

One hundred patients with acute pancreatitis admitted to the General Infirmary of Leeds over a period of six years are analyzed in a study by Pollock (*Brit. M. J.*, 1: 6, 1959). An additional 41 patients were seen in this period, in whom the serum amylase was elevated but whose diagnosis of acute pancreatitis was found to be doubtful or wrong. Of the 71 women 48 had an abnormal gall-bladder whilst of the 29 males the gall-bladder was abnormal in 13. In most cases the abnormality was a cholecystitis with stones. In a number of patients pre-existing intolerance to foods was found, but not one patient was taking alcohol to excess.

In 56 of the cases a correct diagnosis was made from the clinical picture and estimation of serum amylase. Of the nine patients incorrectly diagnosed until necropsy, four were labelled as having coma of uncertain origin, one as a case of anuria due to parathyroidectomy, two as myocardial infarction, one as peritonitis, and one as acute cholecystitis. In 16 of the 35 patients who had a laparotomy, the provisional diagnosis was perforated peptic ulcer; in nine, acute cholecystitis; and in one each, acute appendicitis and strangulated interstitial hernia. In 19 of the 32 who had electrocardiograms taken during the acute attack, the tracing was abnormal and in two of them the diagnosis of myocardial infarction was made. One of these two patients died and no infarct was found. Radiographic examinations such as barium meal examinations may be of diagnostic value if carried out early in the attack. Serum amylase level was elevated above 600 units in 71 of the patients, but it was above this level in eight patients who subsequently were found to have intestinal obstruction, perforated gastric ulcer, empyema of the gall-bladder, myocardial infarction, ruptured ovarian cyst or stone in the common duct. The complications included jaundice, diabetes, tetany, electrolyte disturbance and uræmia, anaemia and hypoproteinaemia, gastro-intestinal hæmorrhage, masses and pseudocysts. Twenty-six of the patients died, the severity of the attack and the age having an obvious bearing on the prognosis. Most of the patients who recovered remained well for one to five years. Resuscitation, antibiotic administration, correction of metabolic and electrolyte disturbances, and use of antitryptic substances and corticosteroids are discussed, but the definite impression is that a mild case will recover irrespective of treatment and that the severe case is not influenced by treatment to any marked degree.

DIAGNOSIS OF GOUT

In a total of 737 patients, serum uric acid was determined by Goldthwait *et al.* (*New England J. Med.*, 259: 1095, 1958) during 1949-1956. In 225 patients, values greater than 6 mg. per 100 ml. were found. Of these, 78 gave a typical history of gout, and nine more were seen in the initial attack of gout. Another 26 patients were diagnosed as having gout although the clinical picture was not typical. Of the remaining 112, rheumatoid arthritis was the diagnosis in 32, in 23 patients atypical rheumatoid arthritis was diagnosed,

and eight patients with psoriasis were also considered to have rheumatoid arthritis. Unrelated joint disease and other unrelated diseases were present in 47 patients, and two had chronic renal insufficiency. Polycythæmia and a family history of gout were considered a possible explanation for hyperuricæmia in less than half the patients without clinical gout. The question of irregular gout is discussed and the difficulty of differentiating atypical gout from atypical rheumatoid arthritis is pointed out. "A good response to an adequate trial of colchicine is evidence of gout." The hyperuricæmia observed in the miscellaneous group may be explained as the random occurrence which is found in over 10% of people over 65 years of age.

CANCER AND BRONCHITIS MORTALITY IN RELATION TO ATMOSPHERIC DEPOSIT AND SMOKE

On the basis of studies of air pollution, population density and standardized mortality from bronchitis, lung cancer and cancer of stomach, intestine and breast in 58 boroughs in England and Wales, highly significant relationships are reported by Percy Stocks (*Brit. M. J.*, 1: 74, 1959). In the administrative areas of Lancashire and Yorkshire, bronchitis is significantly correlated with deposit but not with smoke. The reverse relationship obtains for lung cancer, whose incidence was found to be correlated with population density in adjacent districts, confirming the effect of wind-borne smoke on the incidence of lung cancer.

Stomach cancer is related to both deposit and smoke, probably because food is exposed to dirty air. This could explain the fact that mortality from cancer of the stomach has not shown the same fall in Britain as is being observed in the U.S.A. where food packaging in separate wrappers was introduced long before it became fashionable in Britain. By contrast, cancer of the breast shows no relationship to deposit or smoke, and in the case of cancer of the intestine the relationship is insignificant.

PLEURAL BIOPSY IN DIAGNOSIS OF PLEURAL EFFUSION

Experience with 228 pleural biopsies on 200 patients, most of whom had an effusion at the time of the investigation, is reported by Mestitz, Purves and Pollard (*Lancet*, 2: 1349, 1958). Using the Harefield needle, they obtained punch biopsy specimens of the parietal pleura which were cubes or strips 2-3 mm. long. In four of the 200 patients no adequate specimen was obtained and altogether eight specimens of 223 specimens were unsatisfactory. The results show that pleural biopsy is a simple and safe procedure which can frequently correct a wrong initial diagnosis based on clinical findings and history. Several case histories are presented to illustrate the value of punch biopsy, and various tables show the accuracy of diagnosis by this method. The authors state that it can establish the diagnosis in about 80% of tuberculous and in 60% of malignant effusions. There was only one false diagnosis in the whole series. Punch biopsy should be part of the initial investigation of every case of pleural effusion of uncertain cause.

(Continued on advertising page 56)

NEW DRUGS

This section on drug preparations, presented as an aid to prescribers, consists of two parts. The first consists of monographs on two new products of particular interest, selected and described by competent experts. The second part is a listing of certain new products.

ILOSONE (Propionyl Ester of Erythromycin)

This is a derivative of erythromycin which when given by mouth produces blood levels approximately three times as high as those attained with erythromycin. The main reason for this is that it is not excreted in the bile in significant amounts, and so is retained in the blood stream. It has the same antibacterial spectrum as erythromycin, and presumably shows no enhancement of toxic or sensitivity potential. The recommended dosage is the same as that for erythromycin—i.e. 250 mg. every six hours, and double this amount in severe infections. It remains to be seen whether the higher levels thus obtained will obviate the risk of resistance to the antibiotic developing while treatment continues. This has been one of the difficulties encountered in the treatment of protracted staphylococcal infections in the past. It seems likely that diffusion into the cerebrospinal fluid and brain substance will also be unsatisfactory, although information on this point is not yet available. It should perhaps be emphasized that organisms which have become resistant to erythromycin will also be resistant to Ilosone, so that it must not be regarded as a substitute in this respect.

SULPHADIMETHOXINE (Madribon)

This sulfonamide produces sustained blood levels, so that treatment of susceptible infections can be carried out with one dose per 24 hours. A dose of one gram daily produces an average level of 6 to 8 mg. %. The drug is excreted largely as a glucuronide, which is soluble, and said to have some therapeutic activity. Only 7% of the administered dose appears in the urine in free form. In spite of this, some success has been attained with the drug in the prevention of acute urinary "flare-ups" in paraplegics, but its effectiveness in acute urinary infections remains to be determined. It enters the spinal fluid in small quantities, and may not be suitable for the treatment of meningitis. The incidence of urinary complications of treatment may be expected to be small, and the incidence of the more common sensitivity reactions will probably parallel that of other sulfonamides. Its use has not yet reached a level which will allow this to be evaluated. The sulfonamides are broad-spectrum agents whose action is bacteriostatic, and still serve a useful purpose where bactericidal agents are not required. They are probably not the agent of choice in the treatment of acute streptococcal pharyngitis, for example, if prevention of rheumatic fever is to be accomplished. The recommended dosage is one gram initially followed by 0.5 g. every 24 hours. It is marketed in the form of 0.5 g. tablets or a suspension containing 0.25 g. per teaspoon. The paediatric dose is calculated on the basis that an 80-lb. child receives the same amount as an adult, and smaller children in proportion to their weight.

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This listing of new products is based on information received from Dean F. M. Hughes, Faculty of Pharmacy, University of Toronto, and the *Canadian Pharmaceutical Journal*, to whom we owe thanks.

COMPOCILLIN-VK GRANULES FOR ORAL SOLUTION, (Pr), Abbott

Description.—Soluble, dry preparation of potassium penicillin V. When reconstituted with water according to directions, each 5 c.c. contains: penicillin V (as the potassium salt), 125 mg. (200,000 units) in "cherry-flavoured clear solution."

Indications.—For the treatment of infections amenable to oral penicillin therapy. Also indicated as a prophylactic

agent against recurrence of rheumatic fever, and in the management of rheumatic carditis. May be of value in preventing secondary bacterial infection following acute specific fevers or other viral infections.

Administration.—In acute infections, the initial recommended dose is from 125 mg. (200,000 units) three times daily to 250 mg. (400,000 units) every four hours. Dosage within this range should be adjusted according to the severity of infection and response of the patient.

How supplied.—40 c.c. (1 g.) and 80 c.c. (2 g.) bottles.

AQUIL, (Pr), M. & M.

Description.—Chlorothiazide (6-chloro-7-sulfamyl-1, 2, 4-benzo-thiadiazine-1, 1-dioxide); non-mercurial oral diuretic, primarily a saluretic inhibiting reabsorption of sodium and chloride ions and, to a lesser extent, of potassium and bicarbonate ions.

Indications.—Edema states, e.g. congestive heart failure, cirrhosis, renal edema provided renal blood flow is adequate, toxæmia of pregnancy and pre-eclampsia, and edema from certain drugs, particularly steroids causing sodium retention. Also as an adjunct in treatment of hypertension.

Administration.—250 mg. to 1000 mg. once or twice daily. Mild cases may require only 250 mg. daily in the morning. For severe cases and to initiate therapy 1000 mg. twice daily is equivalent to regular parenteral mercurial therapy in diuretic effect. Patients who have had ganglionic blocking therapy for hypertension should start on only one-half 250 mg. tablet daily for further hypotensive action.

How supplied.—250 mg. tablets, bottles of 100 and 500; 500 mg. tablets, 50 and 500.

ENZADERM Ointment, M. & M.

Description.—Each g. contains: trypsin 5000 tryptic units, chymotrypsin 5000 tryptic units, bacitracin U.S.P. 500 units, polymyxin B sulfate U.S.P. 5000 units.

Indications.—Infected and necrotic wounds suitable for topical therapy.

Administration.—Apply to lesion 1 to 3 times daily, covered if necessary with air-permeable gauze.

How supplied.—15 g. tubes.

OPHTHOCORT Ophthalmic Ointment, (Pr), P. D. & Co.

Description.—Chloromycetin 1%, hydrocortisone acetate 0.5%, polymyxin B sulfate 5000 units per g. in a petrolatum base.

Indications.—Ocular inflammation.

Administration.—Locally 2 to 4 times daily.

How supplied.— $\frac{1}{8}$ oz. tubes.

LOFENALAC, Mead

Description.—Special infant formula product containing balanced dietary nutrients, low in phenylalanine, for use in phenylketonuria. The protein component is a casein hydrolysate from which phenylalanine has been removed.

How supplied.—2 $\frac{1}{2}$ lb. cans.

PHENISTIX, Ames

Description.—Paper strips impregnated with reagents to detect phenylketonuria in infants. The strip is dipped in the urine specimen or pressed against wet diaper. Any colour developing is compared with colour scale on the bottle label after 30 seconds.

How supplied.—Bottles of 50 strips.

"MILPATH" TABLETS, Ayerst

Description.—Each tablet contains: meprobamate (Miltown) 400 mg., tridihexethyl chloride 25 mg.

Indications.—The control of gastro-intestinal disturbance, either caused by or aggravated by anxiety or tension, e.g. gastric and duodenal ulcer, spasm of the oesophagus, spastic and irritable colon (mucous colitis), ileitis, intestinal colic, gastric hypermotility, and anxiety neuroses with vague gastro-intestinal complaints.

Contraindications.—As for any anticholinergic: urinary bladder neck obstruction, pyloric stenosis, and glaucoma.

Administration.—Adults—One tablet at each meal and two at bedtime.

How supplied.—50.

"MILTRATE" TABLETS, Ayerst

Description.—Each tablet contains: meprobamate (Miltown) 200 mg., pentaerythritol tetranitrate (PETN) 10 mg.

Indications.—For prophylaxis of pain in angina pectoris and coronary insufficiency. Not designed for the relief of acute angina pain, but suggested particularly in controlling the anxiety that often accompanies and increases the symptomatology of angina pectoris.

Contraindications.—Given with caution to patients with glaucoma.

Administration.—One or two tablets q.i.d. before meals and at bedtime.

How supplied.—50.

STENISONE, (Pr), Organon

Description.—Each tablet contains: 5 mg. prednisone, 20 mg. methandriol, 100 mg. magnesium trisilicate, 60 mg. dried aluminum hydroxide gel, 70 mg. calcium carbonate, 40 mg. magnesium carbonate, 66.6 mg. Regonol (guar gum), and 30 mg. Egraine (cooked oat flour as binder).

Indications.—For the conservative management of disorders requiring adrenal steroid therapy. Because it includes a nitrogen-sparing anabolic hormone and antacid medication, is suggested in disturbances requiring long-term therapy, such as rheumatoid arthritis, bronchial asthma, lupus erythematosus, gouty arthritis, rheumatic fever, pemphigus, ulcerative colitis and dermatomyositis.

Administration.—Initial dose—4 to 6 tablets (20-30 mg. prednisone) daily. Reduce weekly by 2.5 to 5 mg.

Maintenance dose—1 to 4 tablets (5-20 mg. prednisone) daily.

How supplied.—30.

"NEOSPORIN" LOTION, B. W. & Co.

Description.—Contains polymyxin B and neomycin in a water-miscible, uncoloured and unscented lotion base.

Indications.—Prophylaxis or treatment of mixed bacterial infections of the skin.

How supplied.—20 c.c. plastic squeeze bottle.

"NEOSPORIN" TOPICAL POWDER, B. W. & Co.

Description.—Contains polymyxin B, neomycin and bacitracin in a fine water-soluble powder base.

Indications.—Prophylaxis and treatment of topical bacterial infections where dry therapy is desired.

How supplied.—Shaker-top bottles of 10 g.

NADEINE, (Pr), Nadeau

Description.—Narcotic-analgesic for oral, parenteral and rectal administration, lacking usual side effects of other narcotics such as morphine.

Indications.—Relief of pain after surgery and pain associated with malignancy, and as a supplement to anaesthetics.

How supplied.—Multiple dose vials of 10 ml.

Ampoules of 1 ml. in boxes of 12, 25, 100.

Tablets in bottles of 25, 100, 500.

Suppositories in jars of 12.

Nadeine APC Tablets.—Bottles of 50, 500.

EQUANITRATE, Wyeth

Description.—Each tablet contains: meprobamate 200 mg., pentaerythritol tetranitrate 10 mg.

Indications.—Angina pectoris prophylaxis—dilates coronary vessels and lessens apprehension, anxiety and tension.

How supplied.—50.

NEO-THEPRYL, Will

Description.—Chlorpheniramine maleate, tablets 2 mg. and 4 mg.

Indications.—Allergic states (urticaria, hay fever, contact dermatitis, etc.), pruritus, etc.

Administration.—Adults, 2 to 4 mg. every four hours; children, according to age.

How supplied.—100, 500, 2 x 500.

NEO-THEPRYL EXPECTORANT Syrup, Will

Description.—Each 5 ml. contains: chlorpheniramine maleate 2 mg., ammonium chloride 120 mg., potassium guaiacol sulfonate 60 mg., sodium citrate 60 mg., ephedrine sulfate 4 mg.

Indications.—Coughs due to colds and bronchitis and those of allergic origin.

Administration.—Adults, 1 to 2 teaspoonfuls 3 times daily.

Children, according to age.

How supplied.—16, 80 and 2 x 80 fl. oz.

INFLUENZA VIRUS VACCINE, POLYVALENT, types A & B, Pfizer

Description.—Refined and concentrated, consists of influenza virus, types A and B, propagated in the extra-embryonic fluids of the developing chick embryo. The virus is inactivated by treatment with formalin.

Contains a total of 500 CCA units of virus per c.c., 200 CCA units per c.c. of Asian strain and equal parts of PR 8, PR 301, and Great Lakes.

Administration.—Adult immunizing dose is usually two doses of 1 c.c. given subcutaneously with the second dose given not less than two weeks after the first. For those who, during the preceding six months, have received any injection of influenza vaccine, a single dose of 1 c.c. administered subcutaneously is recommended.

For children under 12 years of age, the subcutaneous immunizing dose should not exceed 0.5 c.c. with proportionately smaller doses for younger children.

The duration of immunity is not known at present, but it may be advisable to give a reinforcing dose at intervals of approximately four months to those who wish to maintain immunity.

How supplied.—5 c.c. vial, five doses.

ANTIVERT, Pfizer

Description.—Each blue scored tablet: meclizine 12.5 mg., with niacin 50 mg.

Indications.—For the relief of vertigo whether due to cerebral arteriosclerosis, Ménière's syndrome, or labyrinthitis or associated with streptomycin therapy. Has also been found effective in treating recurrent headaches, including migraine. Side effects are minimal, mostly limited to the harmless flushing and tingling associated with vasodilation.

Administration.—One tablet before each meal.

How supplied.—100.

DIABINESE, Pfizer

Description.—Chlorpropamide, hypoglycaemic agent for the oral therapy of diabetes; has high potency and long duration of action.

Indications.—In selected diabetic patients, eliminates or decreases the requirements for insulin and provides satisfactory control of the disease. The most likely patient is the one suffering from mild and stable diabetes of the maturity-onset or adult type, inadequately controlled by dietary regulation. In addition, a therapeutic trial may be indicated in: adult-type diabetics with "brittle" control, who may be helped to "smooth" control and lower insulin requirements; primary or secondary failures with previous oral therapy; patients whose degree of control with present oral therapy does not meet the physician's criterion.

Administration.—Most patients are adequately managed by 250 mg. to 500 mg. daily. Complete details available.

How supplied.—Tablets 250 mg., bottles of 30 and 100; 100 mg. tablets, bottles of 100.

DEXTRAN 12% in Abbo-Liter Container, Abbott

Description.—Each 100 c.c. contains: dextran 12 g., sorbitol solution, N.F., as stabilizer 5.7 g., in water for injection, U.S.P. salt-free. For intravenous administration in nephrosis to enhance diuresis and to lessen oedema.

How supplied.—250 c.c. bottles.

(To be continued)

GENERAL PRACTICE

INTRAVENOUS THERAPY IN INFANTS AND CHILDREN*

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IT IS INTENDED in this article to review some of the problems of intravenous therapy in infants and children. This review is not necessarily intended for those already familiar with the subject, but as a guide for those who are not constantly using these techniques.

It has been stated that more seriously ill patients have been saved by the proper use of intravenous therapy than by the use of any other group of substances. Today, intravenous infusions are almost routine in most hospitals; consequently certain techniques, general rules and principles have been established for their safe and proper administration. This article will review some of the problems of administration of water, blood and electrolytes to children, with a discussion on equipment and intravenous solutions. Comments will also be made on specific intravenous therapy in certain diseases in infancy.

EQUIPMENT

A. Solution Units

Intravenous solutions are in bottles containing from 150 to 2000 ml. of the appropriate solution. For infants and children, bottles containing not more than 250 ml. are to be preferred, *as no child under six months of age* should be receiving intravenous fluid from a container larger than 250 ml.

The danger of sudden rapid infusion is always present, in spite of the most careful medical observation. Using smaller-sized bottles, therefore, will help prevent:

- (a) the possibility of intravenous "drowning";
- (b) the possibility of septicæmia, which may occur if the same bottle is used for long periods of time.

B. Intervening "Fluid Traps"

Today, most intravenous tubing is plastic and disposable. In the course of the intravenous tube from the bottle to the infant, there should exist:

- (a) a "drip opening" where fluid drops can be seen and counted;
- (b) an intervening "trap".

The latter consists of a glass or plastic bag† calibrated to contain a maximum of 50 ml. of fluid. After the 50 ml. has been infused, the plastic "trap" will collapse, preventing further fluid from reaching the infant until the bag has been refilled and adjusted under medical supervision. Premature infants, the newborn and young infants require very small amounts of fluid over a 24-hour period. The availability of an intervening "trap" will allow the nurse much better control over the

amount of fluid to be given. It may also be used for administration of specific medication in appropriate dilution. If a Y-tube attachment is also available, two solutions (e.g. 5% glucose and distilled water with equal parts of Darrow's solution) may be suspended and mixed accurately and aseptically by use of the plastic bag.

C. Fluid Balance Chart

All patients receiving intravenous fluids require a proper fluid balance record. Summaries of fluid totals, etc., described in the nurses' clinical notes, are inadequate. Fluid balance charts provide for accurate recording of the type of fluid given, the amount given per hour, the total amount of fluid over 24 hours, and the fluid output. The patient's name, weight, and temperature should be recorded. The recording of blood chemical findings is also worth while. The record should provide the physician or surgeon with sufficient information to assess the patient's condition quickly with regard to water and electrolyte balance.

SOLUTIONS

The number of intravenous solutions available is legion, and to attempt to have on hand in a dispensary all types of intravenous fluids is impracticable. However, certain solutions should be standard, and the following are suggested:

(a) *5 and 10% glucose and water.*—These provide water and calories, the latter being extremely important to seriously ill patients. So-called "invert" mixtures enable one to give twice the number of calories, with perhaps less carbohydrate loss and danger of phlebitis than when 10% glucose is used alone.

(b) *Two-thirds 5% glucose and one-third saline.*—This is a hypotonic solution which may be the first intravenous fluid used in almost all diseases requiring intravenous therapy. It provides water, calories, and some sodium and chloride ions in a concentration much less than in the infant's serum.

(c) *Ringer's lactate solution (Hartmann).*—Diluted with an equal part of 5% glucose in water, this solution is excellent as a maintenance fluid. Because of its mildly alkalizing effect, Hartmann's solution is frequently used in cases of mild metabolic acidosis.

(d) *5% glucose and normal saline.*—This should be available, but in infants and children should not be used in full strength. Dilution with equal parts of 5% glucose and water is to be preferred when administering to young infants. In certain specific conditions where there has been an excess loss of sodium chloride, full-strength 5% glucose and normal saline may be used, e.g. acute adrenal insufficiency, diabetes mellitus or salt-losing nephritis. Even here, hypertonic 3% sodium chloride solution may be necessary.

(e) *Darrow's solution.*—This solution provides potassium in the form of lactate, and is excellent when given in half-strength with 5% glucose and water as a maintenance fluid in cases of gastroenteritis.

(f) *One-sixth molar lactate solution and 3% sodium bicarbonate* are used for the treatment of

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†Available from Baxter Laboratories or Abbott Laboratories.

metabolic acidosis. Sodium bicarbonate is perhaps better than 1/6 M. lactate for the treatment of acidosis, because: (1) the liver is not necessary for its metabolism, and (2) a much smaller quantity of sodium bicarbonate solution (in ml.) may be given than 1/6 M. lactate to produce the equivalent effect.

(g) *Ampoules of calcium gluconate and potassium chloride* should be available. Amino acid solutions are only rarely required.

(h) *Plasma* is extremely useful for combating shock and providing protein. It generally provides all the constituents of whole blood except cells. If it is not available, the plasma volume expanders may be used, e.g., dextran or Intradex.

(i) *Whole blood.*—The administration of whole blood has become routine in most hospitals. Its use should be confined to the treatment of shock, acute blood loss, certain surgical procedures, severe anaemias and blood dyscrasias. The value of administering blood transfusions to seriously ill infants with undiagnosed conditions or severe gastro-enteritis may be questioned. As much good, with much less danger, may be done with plasma as with whole blood. The use of whole blood almost routinely during operative procedures in infants should be discouraged. Frequently the surgeon, physician or anaesthetist ordering blood for an infant may have very little knowledge regarding the actual amount of blood to be given. A 5-lb. infant with a blood volume of 75 c.c. per kg. may well receive twice his or her total blood volume over two to three hours when only a small amount of blood has been lost during the operative procedure. Estimation of the actual amount of blood loss during an operative procedure is extremely difficult and can only be approximate. As a rough guide to the amount of blood lost during an operation, we have assumed a loss of 1 ml. if a two-inch (5-cm.) sponge is bloodstained and 2 to 3 ml. if the sponge is wet. Knowing the number of sponges used, one may replace at regular intervals the calculated amount of blood lost during the operative procedure. Normally, blood should be given in amounts not greater than 10 ml. per lb. of body weight at one time, unless there is marked bleeding. The over-enthusiastic administration of whole blood to young infants with surgical conditions may occasionally account for the statement that "the operation was a success but the patient died."

SPECIFIC INTRAVENOUS THERAPY

Frequently the physician responsible for the ordering of intravenous fluids is not aware of the importance of the way in which he gives or writes his orders for proper instruction to the nurse. It is imperative that orders for intravenous therapy should include:

- (a) the type of fluid to be given;
- (b) the rate per hour (or drops per minute);
- (c) the total amount of fluid to be given over a 24-hour period.

All orders for intravenous therapy should be reassessed at least at the end of each 24-hour period, and new orders written. In infants, postoperatively,

the intravenous therapy should be assessed frequently—at least every six to eight hours. The physician should not expect a nurse to be responsible for ordering the type of fluid or the rate at which it is to be given, when an order is left to "start an intravenous infusion" or "alternate glucose and water with saline".

I. Water

The infant requires a proportionately greater amount of water over a 24-hour period than does an adult. This is because of:

- (a) the larger body surface of an infant compared with body volume;
- (b) high metabolic rate of infants;
- (c) rapidity of fluid turnover;
- (d) functional immaturity of the neonatal kidney.

The suggested water requirements for the normal child are:

(A) Using body weight and age	(B) Using body surface
Premature and newborn infants up to 3 weeks — 90 ml./kg./day	2000 ml. of fluid per m. ² body surface (calculated from a nomogram) (1) (see Table I).
1 year — 150 ml./kg./day	
1 - 2 years — 120 ml./kg./day	
2 - 4 years — 100 ml./kg./day	
4 years — 80 ml./kg./day	

It is important to remember that newborn and premature infants cannot readily excrete large amounts of water and salt, and may quickly become oedematous if not carefully observed.²⁻⁴ Suggested normal daily sodium requirements are:

Birth to 6 months — 0.5 g. or 8 mEq.; or 30 mEq./m. ² /day for newborn, then 50 mEq./m. ² /day.	
1 - 2 years — 1 g. or 17 mEq.	
3 years — 3 g. or 50 mEq.	
10 years — 4 g. or 170 mEq.	

Seriously ill infants, and particularly post-operative patients, may require almost no sodium at first, because of abnormal sodium retention related to increased adrenocortical function and decreased glomerular filtration.

Potassium

Darrow *et al.*⁵ and Mateer *et al.*⁶ have shown by careful observation the presence of marked potassium depletion in cases of acute gastro-enteritis and pyloric stenosis, etc. The clinician must be aware of this abnormal loss of potassium and not rely only on serum concentrations to indicate potassium deficiency. Recent studies with radioactive K⁴² have revealed marked discrepancies between total body potassium and serum concentrations.⁷ Sodium is an antagonist of potassium, and with a constant infusion of solutions containing sodium progressive potassium depletion may occur. Therefore, the use of mixtures containing potassium, such as Darrow's or Butler's solution, is of great value in preventing the occurrence of potassium deficiency during intravenous therapy. Potassium chloride may be added directly to intra-

venous fluids when available, e.g. in ampoules providing 1 ml. = 2 mEq. KCl.

For potassium therapy in conditions of potassium deficiency, we suggest that:

1. Urine output must be established.
2. Three mEq. of potassium per kg. body weight should be given each day.
3. The concentration of potassium in a solution should be less than 40 mEq./litre.
4. The rate of administration should be less than 0.5 mEq./kg. body weight per hour.

Oral administration of potassium is to be preferred, but in conditions of disturbed intestinal function, absorption may be faulty, requiring the intravenous administration of potassium. It requires from four to five days of potassium replacement to correct a deficiency state.

Acidosis and Alkalosis

Most electrolyte disturbances in infants and children result in metabolic acidosis. However, in states of chronic potassium deficiency, made worse by the administration of steroids or large amounts of intravenous sodium, metabolic alkalosis may occur. In acidosis, treatment mainly consists of the administration of 1/6 molar lactate or sodium bicarbonate. We prefer sodium bicarbonate for reasons previously mentioned.

Although one cannot correct exactly to normal an abnormal blood CO₂ or pH by the mathematical calculation of the amount of alkali to be given, we recommend:

(a) Sodium bicarbonate—0.058 g./kg. body weight to raise the CO₂ content 1 mEq. litre, or 0.026 g./kg. body weight to raise the CO₂ combining power by 1 vol. % (given in a 2½-3% concentration).

(b) One-sixth molar lactate—4.2 ml./kg. body weight to raise the CO₂ content 1 mEq./litre, or 1.8 ml./kg. body weight to raise the CO₂ C.P. 1 vol. %.

It is well not to attempt to correct the CO₂ content by more than 8 mEq. at one time.

TABLE I.—SURFACE AREA (M.²) RELATED TO BODY WEIGHT (KG.)

(Assuming child is of average height and weight for age)

Wt. in kg.	S.A.	Wt. in kg.	S.A.	Wt. in kg.	S.A.
1.0	.10	6	.33	14	.61
1.5	.12	7	.38	15	.64
2.0	.15	8	.42	16	.71
2.5	.18	9	.45	17	.74
3	.20	10	.49	18	.76
4	.25	11	.52	19	.79
5	.29	12	.55	20	.82
		13	.58		

S.A.—Surface area.

Using surface area (Table I), the same solutions may be given using 360 ml./m.² for replacement of fluid deficit over one hour, followed by maintenance fluid intake of 2500 ml./m.² for the remaining 22 hours and 2000 ml./m.² per day thereafter. If abnormal fluid loss continues, this should be estimated and added to the calculated fluid requirements.

TABLE II.—INTRAVENOUS TREATMENT OF ACUTE GASTRO-ENTERITIS WITH SEVERE DEHYDRATION

(A) Hypotonic dehydration	(B) Hypertonic dehydration
(1) Start an intravenous infusion of 1/2 strength Ringer's lactate (Hartmann's) solution at 20 ml./kg./hr. for two hrs.	(Serum sodium level above 150 mEq./litre). (1) Give an intravenous infusion of 1/3 strength Ringer's lactate solution or 1/3 strength normal saline (with 5% glucose and distilled water) at a rate of 180 ml./kg. over 24 hours.
(2) The child should void by the end of two hours; then give equal parts of Darrow's solution, with 5% glucose and distilled water at 10 ml./kg./hr. for 12-18 hours.	N.B.—Avoid rapid infusion. (2) Give calcium gluconate 0.5 to 1 g. in two hours and repeat twice a day.
(3) Oral fluid may be started after 12 hours, beginning with sugar water.	(3) Potassium may be given in amounts of 1½ to 2 mEq./kg./day after two hours.
(4) The intravenous infusion can usually be discontinued after 24 hours.	(4) Watch for convulsions.

POSTOPERATIVE INTRAVENOUS FLUIDS FOR INFANTS

In general young infants, particularly premature and newborn requiring surgical procedures, appear to do better postoperatively when intravenous fluids have been kept to a minimum preoperatively to avoid overhydration.⁸ The over-administration of intravenous infusions postoperatively may well be the cause of death in newborn infants when the clinical picture is that of pneumonia.⁹

Postoperatively, Gross¹⁰ has suggested the administration of 30 ml./lb. of body weight over 24 hours, while Swenson¹¹ has suggested 1200 ml./m.² body surface. The metabolic changes occurring postoperatively in adults, as described by Moore,¹² consist of sodium and chloride retention, anti-diuresis and potassium loss. Insufficient studies have been carried out for an accurate description of the changes occurring in infants. However, it seems from the work of Rickhan¹³ and more recently of MacLean and Paulsen¹⁴ that sodium and chloride retention is not as marked as in adults, and anti-diuresis is less evident. However, it is suggested that fluids be restricted to 30 ml. per lb. and sodium intake restricted to ½ mEq./lb. body weight for the first 24 hours.

Potassium should be administered in amounts of ½-1½ mEq./lb./day after the first 24 hours. Increased intake of water, sodium chloride and potassium may be necessary if abnormal losses continue postoperatively, e.g. by ileostomy, vomiting, gastric suction. After the second day, normal fluid and electrolyte requirements may be given with close observation.

It is most important that seriously ill infants receive adequate calories. Because of the limitation of providing adequate calories by the intravenous route, oral feeds should be given as soon as possible.

SUMMARY

A brief review of the problems of intravenous therapy related to infants and children is presented.

The recommendations and suggestions are based on the present knowledge of fluid and electrolyte balance in infants only, and are not necessarily applicable to adults. It is hoped that the tendency to overhydration

and over-administration of sodium to infants may be abolished.

We firmly believe that not only will the infant mortality of gastro-enteritis and other diseases requiring intravenous therapy be reduced, but a further lowering of the morbidity with a shortening of the infant's stay in hospital will result, if these general rules and principles are applied.

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Association Notes

W.M.A. PRESIDENT NOMINATED

The many friends of Dr. Renaud Lemieux of Quebec City will be gratified to hear that at the recent meeting of the Executive Committee of the Canadian Medical Association, a ballot resulted in his nomination as President of the World Medical Association. This Presidency fell vacant through the death of the President-Elect, Dr. Gérin-Lajoie. It is expected that the nomination will be confirmed at the meeting of Council of the World Medical Association in Sydney, Australia, later this month.

LORD ADRIAN TO ADDRESS THE EDINBURGH MEETING

One of the highlights of the British Medical Association's Annual Meeting is the Presidential Address, which is usually given on the Monday evening of the week in which the scientific sessions are held. Unfortunately, as has been mentioned previously in these columns, the Duke of Edinburgh will be unable to be present on this occasion to deliver his Presidential Address. The latter will be given by His Royal Highness at his installation in Toronto at some date still to be fixed.

However, it is a pleasure to record that Lord Adrian, the distinguished British scientist, has accepted an invitation to address the Adjourned Annual General Meeting on Monday evening, July 20. It is also a pleasure to announce that Dr. Wilder Penfield of Montreal is making a special trip to Edinburgh to move a vote of thanks to Lord Adrian on this occasion. *

C.M.A. EXECUTIVE COMMITTEE

The Executive Committee of the Canadian Medical Association met at C.M.A. House, Toronto, on February 20 and 21, with Dr. Norman H. Gosse in the Chair. The meeting opened with a tribute to the late Dr. Léon Gérin-Lajoie by the Chairman, and at the request of the Committee a record was entered on the minutes expressing the C.M.A.'s gratitude for his valuable work and their sorrow at his passing.

The minutes of the last meeting, October 31 and November 1, 1958, were adopted. It was announced that Dr. Duff Wilson had accepted the post of Chairman of the Committee on Public Health, and Dr. L. O. Bradley the Chairmanship of the Committee on Hospitals for Intern Training.

Because of the valuable work previously done by Dr. Frank Turnbull of Vancouver on the Committee on Organization, the Executive decided to ask Dr. Peter Lehmann of Vancouver to take over the Chairmanship of that Committee, relinquished by Dr. Turnbull. In this way, the new Chairman would have the benefit of the previous Chairman's advice.

Progress was reported on the Bill presently before the Federal Parliament to amend the Act of Incorporation of the Canadian Medical Association, so as to enable it to broaden the scope of its activities. The Committee was informed that on February 13, 1959, Mr. H. M. Horner (Jasper-Edson) had moved the second reading of the Bill; the motion was agreed to, and the Bill read a second time and referred to the Standing Committee on Miscellaneous Private Bills.

There was an extended debate on a request from the Canadian Association of Radiologists, who had asked the Canadian Medical Association to assume some of the responsibility for an approval program for schools for radiological technicians. It was agreed that Dr. Edward A. Petrie of Saint John, N.B., should be asked to chair a new Standing Committee of the C.M.A., the other members of whom would be nominated by the Canadian Association of Radiologists. This committee would elaborate a basis of approval of schools for radiological technicians, for adoption by the General Council. It was also agreed that the C.M.A. should nominate a representative to the Joint Committee of the Canadian Association of Radiologists and the Canadian Society of Radiological Technicians. A contingency fund was voted to set up the new C.M.A. Standing Committee.

Advisory Committee to the Federal Government

The C.M.A. Advisory Committee to the Federal Government had met with government representatives in Ottawa on February 19 and discussed three main topics. There had been an exchange of information on the work of the Indian and Northern Affairs Department. A statement prepared by the C.M.A. Head-

quarters was given to the Department of National Health and Welfare; this statement described the attitude of the medical profession as represented by the C.M.A. to the federal-provincial hospital insurance plans. Great stress was laid on the fears of the profession that the plans might operate to the detriment of medical education. The Advisory Committee was reassured that this thought was in the minds of the Government also. Thirdly, in view of the fact that the Canada Shipping Act may be amended soon, the C.M.A. Committee asked that they be given a chance to submit a brief on the medical aspects of this Act at an appropriate moment; reassurance was given that this would be borne in mind.

Canadian Council on Hospital Accreditation

Dr. Kirk Lyon described the inauguration of the all-Canadian program for hospital accreditation on January 17 and the present position of the program.

House Committee

Dr. T. C. Routley brought in the report of the House Committee, and showed detailed plans for construction of the new wing of C.M.A. House. It is possible that the new premises may house the whole of the C.M.A. headquarters staff, leaving space in the old building for rental purposes to associated bodies.

Report of Honorary Treasurer

Dr. G. W. Halpenny read the report of the Honorary Treasurer. He said that the Association had had a successful year, mainly for three reasons: (1) advertising in the Journals had not experienced a substantial reduction during the recent recession, and indeed advertising revenue had increased in 1958; (2) income from fees had increased slightly; (3) expenditures in the Secretariat had not quite reached expected levels. This successful year was a very fortunate thing, because it enabled allocation of sums to the building fund and prevented the selling of C.M.A. securities at a loss in order to complete building financing arrangements.

C.M.A. Publications

Dr. T. C. Routley, Managing Editor, presented his report to the Executive Committee, noting that 1958 had been a successful year financially for the *Canadian Medical Association Journal* and that the new *Canadian Journal of Surgery* had ended the year's operations with a small positive balance. Dr. Routley also described exploratory studies of the possibility of starting a second specialized journal, to deal with internal medicine and clinical investigation, and said that after a thorough canvass of the situation had been made, the Executive would be advised whether or not the second specialist journal might be launched. The possibility of weekly publication of the *Canadian Medical Association Journal* was also under constant review. In adopting this report, the Executive Committee paid a tribute to the sterling work of the Managing Editor.

The Editor, Dr. Gilder, quoted progress with the journals. He referred to the new section in the *Canadian Medical Association Journal* on new drugs and to the introduction of a bilingual title for the Journal on March 1. He also described the recent meeting of the Editorial Board of the *Canadian Journal of Surgery* in Vancouver, and the enthusiastic work this Board was doing for the new surgery journal.

Dr. A. D. Kelly informed the Executive Committee that Volume II of the official *History of the Canadian Medical Association* had recently appeared. This was the work of the C.M.A.'s official historian, Dr. H. E. MacDermot. As a further instance of Dr. MacDermot's industry, Dr. Kelly remarked that he was currently beginning work on a survey of a century of Canadian medicine, 1867 to 1967, in readiness for the centenary meeting in 1967. Members of the Executive Committee asked whether it was possible to consider reprinting Volume I of the official *History*, a book now out of print, and almost unobtainable. The feasibility of this will be inquired into.

Annual Meeting 1959

It was agreed that the next meeting of the Executive Committee of the C.M.A. should take place in Toronto on May 27 and 28, and that this would be immediately followed by the meeting of General Council on May 29 and 30. This in turn would be followed by a second meeting of the Executive Committee on Sunday, May 31. These dates were chosen because they would coincide with the meeting of the Ontario Medical Association.

The Annual General Meeting and installation of the President would take place in Toronto on a date to be arranged by the co-ordinator of the Royal Tour in Canada. Those responsible for the Royal Tour had indicated that the Canadian Medical Association could have the services of their President-elect, His Royal Highness, The Duke of Edinburgh, between the hours of 11:30 a.m. and 2 p.m. on the date arranged. A Sub-committee on Protocol reported on a timing which had been worked out for the occasion. This would essentially be a C.M.A. occasion, without outside participation. The new President would be installed by Dr. VanWart, and Dr. Kirk Lyon would be installed as Deputy to the President.

The program of the B.M.A.-C.M.A. Conjoint Meeting in Edinburgh, July 18-24, was described in detail, with particular reference to the social program.*

British Commonwealth Medical Conference

The British Commonwealth Medical Conference will be held at B.M.A. House, London, on July 11-14, 1959. The Executive nominated Dr. Kirk Lyon as their representative to this conference, with Dr. A. D. Kelly as alternate.

World Medical Association

Arrangements for the XIII General Assembly of the World Medical Association in Montreal, September 7-12, 1959, were discussed. The following C.M.A. delegates to the Assembly were nominated: Dr. N. H. Gosse and Dr. Morley Young; alternates, Dr. T. J. Quintin and Dr. Lorne Whitaker. Dr. J. A. McMillan was appointed as chairman of the Canadian Supporting Committee to the World Medical Association. A closed ballot for the nomination of the presidency of the World Medical Association, vacant on account of the death of Dr. Gérin-Lajoie, resulted in the election of Dr. Renaud Lemieux of Quebec City by a majority.

Dr. G. W. Halpenny reported findings of the sub-committee on W.M.A. finance, and brought in a

*We hope to print this program in full in our next issue.
—Editor.

recommendation that next year's contribution to the World Medical Association through the Canadian Medical Association should be \$9000. Dr. Routley, Chairman of the Planning and Finance Committee of the W.M.A., said that this Committee had worked out a new assessment for all member associations of the W.M.A. based on units of \$1000. The assessments range from 125 units from the American Medical Association (a figure already accepted by the latter), through 15 units for Western Germany, 11.5 units for Great Britain, 10 units for Canada and so on down to very small assessments for small and impoverished medical associations. The assessments were based on gross national product and some other factors. It was finally agreed that the Canadian contribution to W.M.A. should be \$10,000, with the understanding that this represented the contribution from all sources, including funds donated to the Canadian Supporting Committee.

The Executive Committee was also asked to consider a motion to be brought before the Assembly this year that German be added as another official language. The Committee agreed that the working languages should remain as at present, namely English, French and Spanish, but the delegates should be permitted to speak in any other language provided they were responsible for interpretations.

Senior Members

The following senior members were elected: Dr. Gordon Burke and Dr. Theodore H. Lennie, Vancouver; Dr. Wallace W. Cross and Dr. John J. Ower, Edmonton, Alberta; Dr. H. C. George, Regina, Saskatchewan; Dr. A. T. Mathers, Winnipeg, Manitoba; Dr. F. A. Brockenshire, Windsor, Dr. G. A. Campbell, Ottawa, Dr. T. C. Routley, Toronto, Dr. W. E. Gallie, Toronto, Dr. H. M. Yelland, Peterborough, Ontario; Dr. Roméo Roy, Levis, and Dr. S. Graham Ross, Montreal, P.Q.; Dr. C. J. Veniot, Bathurst, New Brunswick; Dr. J. C. Ballem, New Glasgow, Nova Scotia; Dr. John Burke, Grand Bank, Newfoundland. No appointment was made for Prince Edward Island.

Trans-Canada Medical Plans

Dr. Murray Douglas read the report of his Subcommittee on T.C.M.P. and this was discussed at length. The report was accepted with slight amendment, and its contents will be discussed with T.C.M.P. in the near future.

Medical Economics

Dr. K. S. Thomson, Chairman of the Committee on Medical Economics, read a brief report of the last meeting of the Committee. Another meeting was scheduled for March 6 and 7.

Funds for Medical Students

A proposal had been before the last meeting of the Executive Committee for the establishment of a bursary or bursaries by the C.M.A. to assist medical students. The Secretariat had investigated the funds available in various divisions across Canada for assistance of students. A preliminary examination of the situation had revealed that a considerable variety of agencies in Canada provide loans, bursaries and scholarships for undergraduates in medicine on the basis of scholarship or financial need or both. It was also noted that large capital sums are required to sustain a loan fund, and that its administration is

complex. In debate of this survey by the Executive Committee, it was suggested that all the money presently available is not being used. Discussion gradually shifted from a consideration of financial aid to a consideration of the reasons why concern was being expressed in various parts of Canada at the quantity and the quality of entrants to medical faculties. This question is being currently pursued by the C.M.A. Committee on Education and the Committee on Public Relations.

Canadian Joint Committee on Nursing

The Executive Committee endorsed a resolution from the Canadian Joint Committee on Nursing which asked that, in view of increasing demands for nursing services and in view of the increased number of potential trainees in nursing (due to the increased birth rate), the Canadian Joint Committee on nursing recommend to its constituent organizations that the Federal and Provincial Governments be approached directly and through provincial members or divisions to give further assistance in the provision of additional facilities and staff for the training of nursing personnel.

Public Relations

Mr. Kenneth Cross, Assistant Secretary (P.R.), read the report on C.M.A. public relations activities. This included a description of the C.M.A. approach to the Federal Parliament. The C.M.A. Advisory Committee to the Federal Government had met with Government on February 19, and an informal meeting had been held in Ottawa on January 29 with physician members of the House of Commons and representatives of the Public Relations Committee. The object of the meeting was to acquaint all concerned with current C.M.A. activities on behalf of the medical profession. A series of information bulletins will be prepared to explain to legislators the attitude of the medical profession to various aspects of hospital insurance. The first of these bulletins was studied by the Executive Committee, and its bilingual distribution was recommended. The next bulletin will particularly concern itself with the problems of university faculties of medicine and teaching hospitals. Information bulletins will be distributed to legislative bodies at the federal and provincial level.

The subject of medical recruitment is under consideration by the C.M.A. Committee on Medical Education, by the Public Relations Committee and by the Association of Canadian Medical Colleges.

Mr. Cross reported, in connection with the Public Educational Program, that production will soon begin on the making of three one-minute TV filmettes showing the Canadian doctor in action—in the home, in the hospital, in the research laboratory. One objective of these filmettes is to stimulate interest of secondary-school students in medicine as a career. The C.M.A. has once more been invited by the *Toronto Globe and Mail* to arrange for publication of a series of ten articles on a variety of health topics. The C.M.A. is also co-operating with the National Film Board in their TV series featuring medicine. Two films are under way, one on retarded children and one on cancer.

Midwinter Secretaries' Conference

The midwinter Secretaries' Conference held on February 6 and 7, 1959, was summarized for the benefit of the Executive Committee.



Divisional Secretaries of the C.M.A. at the midwinter conference. Left to right, standing: Mr. Basil McLaughlin, Assistant Secretary (Public Relations), Ontario; Mr. Jean-Marc Denault, Director of Public Relations, Quebec; Dr. S. S. B. Gilder, Editor, *C.M.A. Journal*; Mr. Kenneth C. Cross, Assistant Secretary (Public Relations), C.M.A., Toronto; Dr. G. W. Halpenny, Honorary Secretary, Quebec; Dr. A. F. W. Peart, Assistant Secretary, C.M.A., Toronto; Dr. F. L. Whitehead, Secretary, New Brunswick; Dr. M. R. Dufresne, Assistant Editor, *C.M.A. Journal*; Dr. C. J. W. Beckwith, Executive Secretary, Nova Scotia; Dr. J. W. Moreside, Honorary Secretary, P.E.I.; Dr. J. Kettlewell, Assistant Secretary, Alberta; Mr. B. E. Freamo, Assistant Secretary (Economics), C.M.A., Toronto; Dr. C. U. Henderson, Honorary Secretary, Newfoundland; Dr. Douglas Kinnear, Assistant Secretary, Quebec; Dr. J. C. Allison, Assistant Secretary, Ontario; Mr. Andrew Gillies, Executive Secretary, Ontario; Dr. Glenn Sawyer, General Secretary, Ontario; Mr. Dorwin Baird, Director of Public Relations, British Columbia. Left to right, seated: Dr. G. Gordon Ferguson, Executive Secretary, British Columbia; Dr. Wm. Bramley-Moore, Secretary-Treasurer, Alberta; Dr. A. D. Kelly, General Secretary, C.M.A., Toronto; Dr. G. W. Peacock, Secretary, Saskatchewan; Dr. M. T. Macfarland, Executive Director, Manitoba.

Other reports heard by the Executive Committee included one on the survey of salaried physicians which is being undertaken by the C.M.A.; the report of Dr. Morley Young, the C.M.A. representative on the Advisory Committee on Medical Research; and the report of the Committee on Approval of Hospitals for the Training of Junior Interns.

Service of Officers

Because of the unusual nature of the C.M.A. Annual Meeting this year, which really includes three separate occasions, in May, June and July respectively, the Executive Committee considered at what point in 1959 the change-over of offices and members of committees should take place. It was finally agreed that the present officers and members of the Executive Committee should serve until the end of the B.M.A.-C.M.A. Conjoint Annual Meeting on July 24, although the present President of the C.M.A., Dr. VanWart, would relinquish his office to the Duke of Edinburgh on his installation and would then become the immediate Past President. It has also agreed that the successors to officers and Executive Committee members would be asked to attend the Executive Committee meeting scheduled to take place on May 31, after the meeting of the General Council.

MIDWINTER SECRETARIES' CONFERENCE

The midwinter Provincial Secretaries' Conference was held at C.M.A. House on Friday and Saturday, February 6 and 7, 1959. The chair was taken by Dr. A. D. Kelly, and the following Provincial representa-

tives were present: *British Columbia*, Dr. G. G. Ferguson and Mr. D. Baird; *Alberta*, Dr. W. Bramley-Moore and Dr. J. Kettlewell; *Saskatchewan*, Dr. G. W. Peacock; *Manitoba*, Dr. M. MacFarland; *Ontario*, Dr. G. Sawyer, Dr. J. Allison, Mr. A. Gillies and Mr. B. McLaughlin; *Quebec*, Dr. G. W. Halpenny, Dr. D. Kinnear and Mr. J. Denault; *Nova Scotia*, Dr. C. J. W. Beckwith; *New Brunswick*, Dr. F. Whitehead; *Prince Edward Island*, Dr. J. W. Moreside; and *Newfoundland*, Dr. C. Henderson.

The meeting began with a discussion of the current status of divisional membership, of fees and of membership promotion schemes. The British Columbia representatives displayed copies of the physician's administrative manual which they had prepared. The forthcoming program for divisional annual meetings and the program for the conjoint meeting of the British Medical Association and Canadian Medical Association in Edinburgh were discussed. Arrangements for the World Medical Association General Assembly in Montreal next September were also described.

The participants devoted much time to consideration of various aspects of medical economics including welfare medical service, present state of hospital and diagnostic services in the provinces, and the current survey of salaried physicians by the C.M.A., the relative value study already begun by the C.M.A., the present status of the C.M.A. Retirement Savings Plan, the working out of uniform Life Insurance Claim Forms (Dr. C. Gossage attended at this point, and discussed the matter with participants), the work of the information centre on medical economics at C.M.A. House, and the whole field of liaison between divisions and the national body on one hand, and governments on the other.

Public relations activities in the divisions and at C.M.A. Headquarters were reviewed. One of the highlights at this discussion was a description of arrangements made by the Ontario Medical Association for a health exposition next October. This will take place in the Queen Elizabeth Building, C.N.E. Grounds, Toronto, and is expected to attract much public interest. Divisional and national medical publications were briefly reviewed and a number of smaller items of business were dealt with.

This meeting was the best attended one so far, and appeared to be the most informative and valuable one to date.

MEDICAL MEETINGS

CONFERENCE ON CEREBRAL PALSY

A comprehensive conference on problems relating to cerebral palsy will be held in Montreal on October 21, 22 and 23, 1959. Separate programs of interest to physicians and surgeons, psychologists, physiotherapists, social workers, occupational therapists, teachers and speech therapists, as well as persons interested in developing programs for the handicapped, will be provided. Discussions of advances in medical and surgical treatment, and ward rounds will be arranged for visiting physicians and surgeons. Advance registration will commence in September.

Further information may be obtained on request from the sponsors: The Cerebral Palsy Association of Quebec, Inc., 1421 Mackay Street, Montreal 25, Que., who are holding this meeting to celebrate their tenth anniversary.

CANADIAN ASSOCIATION OF RADIOLOGISTS

At the 22nd Annual Meeting of the Canadian Association of Radiologists, held in Saskatoon in January, the following officers were elected for the year 1959: President, Dr. E. M. Crawford; Vice-President, Dr. A. E. Childe; Honorary Secretary-Treasurer, Dr. Robert G. Fraser; Associate Honorary Secretary-Treasurer, Dr. Jean-Louis Léger.

PUBLIC HEALTH

A NEW LOOK IN COMMUNICABLE DISEASE REPORTING

Communicable disease reporting has always been a bugbear with practising physicians and statisticians alike. Physicians were unhappy because of what appeared to be useless paper work and red tape; epidemiologists and statisticians were frustrated because the data they got were too incomplete to supply reliable statistics. Reporting of communicable diseases by physicians has been quite complete and accurate

for some of the major diseases, but it has been very incomplete for such diseases as the "childhood diseases". At one time these diseases constituted a serious public health problem; now they are no longer considered sufficiently serious and amenable to public health measures to warrant the inconvenience of reporting each individual case. Public health authorities as well as statisticians, therefore, have been taking another look at the present system of reporting with the objective of making it more realistic and adequate to serve today's public health problems in the field of communicable diseases.

While the methods of reporting are still under study, the first logical step was to review the list of diseases notifiable under provincial legislation.

A new uniform list for adoption by all provinces was prepared with the objective of eliminating the so-called minor diseases considered as deadwood in the old list; these, it was felt, accounted for much of the reluctance in reporting on the part of the practising physician. Such a new list was first recommended by the meeting of provincial and federal health officers in 1955 and, with some revisions, was approved and adopted by the Dominion Council of Health at its 74th meeting in October 1958.

To determine the diseases to be reported in a province is entirely a matter for provincial legislation. While some provinces have already adopted the new list or are going to implement it in their regulations in the near future, others will wish to retain certain diseases not contained in the new uniform list (e.g., measles) or continue to use the old terminology (e.g., non-paralytic poliomyelitis instead of viral or aseptic meningitis).

The new list has been used for the weekly statistical reports from the provincial health departments to the Dominion Bureau of Statistics since the beginning of this year. The new list may still appear rather lengthy, but closer scrutiny will reveal that it omits many of the diseases which in the past formed the bulk of the physician's load of notification. Based on past experience, a physician will encounter in a year on the average only three to four cases of the diseases in the new list. This average may be exceeded where local outbreaks occur, but complete reporting will still require only a very small amount of paper work. Another feature of the new list is that it brings terminology in line with modern epidemiological thinking, for example, by replacing "non-paralytic poliomyelitis" with "viral or aseptic meningitis".

Compared with the old list, the new one shows the following changes:

Deletions	Additions
Actinomycosis	Diarrhoea of the newborn, epidemic (764)
Cancer	Food poisoning:
Chickenpox	(a) Staphylococcus intoxications (049.0)
Conjunctivitis	(b) Salmonella infections (042.1)
(non-gonorrhoeal)	(c) Unspecified (049.2)
Erysipelas	Pemphigus neonatorum (Impetigo of the newborn) (766)
Glanders	Relapsing fever, louse-borne (071.0)
Influenza	Rickettsial infections:
(epidemic)	(c) Q-Fever (108 part)
Measles	Tetanus (061)
Mumps	
Puerperal	
septicaemia	
Rubella	
(German measles)	
Trachoma	
Vincent's angina	

Apart from these changes in the list of notifiable diseases, other improvements in regard to reporting forms and procedures are now under discussion.

SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES— WEEK ENDING FEBRUARY 7, 1959

INFECTIOUS HEPATITIS

BRITISH COLUMBIA—Eighty-seven cases of infectious hepatitis have occurred at the Woodlands School for mental defectives, New Westminster, between January 9 and 26. Twenty-seven members of the staff were affected and 60 patients, male and female, ages 8 to 26 years. The total patient population is 2100. The outbreak was originally confined to one ward of 65 patients. All the patients and staff on this ward received gamma globulin. The infection has spread to other wards among patients and staff.

ALBERTA

Perryvale, Alta.—The Athabasca Health Unit has reported six cases of infectious hepatitis and three suspects. All immediate family contacts were given gamma globulin.

Edmonton, Alta.—During December 1958, there were 34 cases of infectious hepatitis in the Edmonton Indian Agency of which 28 were in children. Seven cases were reported in November 1958.

Slave Lake, Alta.—At Slave Lake there have been 19 cases of infectious hepatitis. Five members of one family were affected and three cases occurred in each of two other families. Eight more cases occurred in December 1958.

MUMPS

Slave Lake, Alta.—About 25 cases of mumps affecting 60% of the children under 15 years of age have occurred in this village. There were a few cases among adults also. Five cases, three in adults and two in children, were complicated by encephalitis.

DIPHTHERIA

Eckville, Alta.—Red Deer Health Unit reports three more cases of diphtheria following a previously reported fatal case in a 3-year-old child. The patients were a 5-year-old boy, who died, a 44-year-old woman and her 6-year-old daughter. None of them had ever been immunized.

UPPER RESPIRATORY INFECTION

Wainwright, Alta.—The Minburn-Vermilion Health Unit reports a second outbreak of upper respiratory infection affecting mostly infants. Fifteen babies under the age of one year have been admitted to hospital. Some had pyrexia while others did not. Various antibiotics have been tried with little effect. The relapse rate is 100% and several babies have had up to three or four relapses. The infection appears to be viral in origin. The blood picture showed a predominance of lymphocytes. Specimens have been sent for laboratory investigation.

INFLUENZA

NEWFOUNDLAND—Further to the previous notification of influenza at Bay d'Espoir, outbreaks of the same virulent type have been reported from two other districts. In St. Joseph's, St. Mary's Bay, there have been three cases affecting three brothers, living separately, who in turn had severe influenza with heavy night sweats, chest pains and bronchitis. One developed bronchopneumonia. Five cases in Long Harbour were all complicated by bronchopneumonia.

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA* ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	Week ended (1959):			Cumulative total since beginning of year	
	Jan. 17	Jan. 24	Jan. 31	1959	1958
Brucellosis (undulant fever).....	(044)	—	1	—	4
Diarrhoea of the newborn, epidemic.....	(764)	—	—	—	—
Diphtheria.....	(055)	—	2	3	2
Dysentery:		23	16	65	49
(a) Amoebic.....	(046)	—	5	1	—
(b) Bacillary.....	(045)	23	14	62	49
(c) Unspecified.....	(048)	—	4	2	—
Encephalitis, infectious.....	(082.0)	—	—	—	—
Food poisoning:		3	7	19	50
(a) Staphylococcus intoxication.....	(049.0)	—	1	1	—
(b) Salmonella infections.....	(042.1)	3	6	16	50
(c) Unspecified.....	(049.2)	—	1	2	—
Hepatitis, infectious (including serum hepatitis).....	(092, N998.5)	70	124	601	167
Meningitis, viral or aseptic.....	(080.2, 082.1)	—	1	2	2
Meningococcal infections.....	(057)	6	3	19	32
Pemphigus neonatorum (impetigo of the newborn).....	(766)	—	—	—	—
Pertussis (whooping cough).....	(056)	155	122	514	526
Poliomyelitis, paralytic.....	(080.0, 080.1)	1	—	2	3
Scarlet fever and streptococcal sore throat.....	(050, 051)	447	655	2093	1103
Tuberculosis:		91	70	285	547
(a) Pulmonary.....	(001, 002)	48	51	182	420
(b) Other and unspecified.....	(003-019)	43	19	103	127
Typhoid and paratyphoid fever.....	(040, 041)	2	3	5	16
Veneral diseases:		363	319	1284	1412
(a) Gonorrhoea.....	(030-035)	322	265	1115	1225
(b) Syphilis.....	(020-029)	41	54	169	187
(c) Other†.....	(036-039)	—	—	—	—

*Excluding Northwest Territories. Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.

†Including chancroid, granuloma inguinale and lymphogranuloma venereum.

SCARLET FEVER

INDIAN AND NORTHERN HEALTH SERVICES

Schefferville, Quebec—Eighteen cases of scarlet fever and three suspects have occurred at Knob Lake among the Fort McKenzie and Sept Iles Indians. It is believed that the infection was introduced to the reserve by a non-Indian. The reserve is under complete quarantine and the town is out of bounds to all contacts, including all Indians, teachers, and medical and nursing personnel. Exception is being made for those workers who have received penicillin prophylaxis for four days. It would appear that eventually the entire Indian population in the reserve may contract the disease. The isolation of patients is almost impossible. Adequate therapeutic and prophylactic measures are under way.

SMALLPOX

GERMANY—The WHO Weekly Epidemiological Record reports that a total of 23 cases of smallpox have occurred in Germany since December 5, 1958, when the first case was notified. Twenty-one were reported in Heidelberg (last case on January 21, 1959), one in Kaiserslautern (December 25, 1958) and one in Köln (January 28, 1959).

STANDARD CYANMETHÆMOGLOBIN SOLUTIONS

The Laboratory of Hygiene, a division of the Department of National Health and Welfare, Ottawa, announces that standards for the determination of hæmoglobin will be distributed free to laboratories on request. These cyanmethæmoglobin standards will be supplied in three dilutions to facilitate use. Anyone wishing to be included on the mailing list for these solutions (when available) should write to the Laboratory of Hygiene, stating the make and model of the instrument that will be used for hæmoglobin determinations.

LETTERS TO THE EDITOR

THE MASTER TWO-STEP TEST

To the Editor:

Permit me, sir, to comment on the paper "A Clinical Re-evaluation of Master's Two-Step Test" (*Canad. M. A. J.*, 80: 9, 1959). I respectfully submit that the organization, selection and classification of the material presented do not, in my opinion, justify the conclusions. Also, in his review of the pertinent literature, the author omitted all reference to recent statistically significant studies corroborating the value of the two-step test.¹⁻³ Finally, the electrocardiograms offered in support of one of the major conclusions are, I am sorry to say, erroneously interpreted.

The paper is an "analysis of 131 Master tests carried out in our ECG department". On this basis, and despite the admission that "one of the most difficult problems facing any physician is the evaluation of atypical chest pain in middle-aged men and women", the material was arbitrarily classified into four groups as follows: (a) angina, (b) possible angina, (c) chest pain (not angina), (d) no chest pain (miscellaneous). The author does not indicate by whom these diagnoses were made, what criteria were used, over what period of time the patients were followed, and how many

different physicians participated in the study. The validity of the Master test is then measured in terms of its correlation with these "impressions". For example, in Group C, labelled "Chest Pain, Not Angina", and described in no greater detail than "patients with a miscellaneous collection of chest pains *not considered* to be anginal in character", 30.2% had positive tests. It is entirely conceivable, perhaps even likely, in view of the protean nature of the symptoms of coronary artery disease, that one-third of a group of patients with "miscellaneous chest pains" do indeed have an anginal syndrome! The implication that the 30.2% positive tests are for the most part "false positives" is, therefore, only speculation.

Conclusions drawn from each of the other groups are equally suspect. For example, Group A ("Angina") is said to demonstrate only 57.7% positive tests by Master's criteria (and only 26.9% positive tests using Simonson's method of interpretation). It is crucial to know whether double "two-step" tests were done in every case. The author states that "single or double tests were carried out after due clinical consideration". According to Master, however, a negative single test does not exclude coronary artery disease; a negative double (three-minute) test does.⁴ Many patients with the anginal syndrome have negative single tests but positive double tests. None of the published electrocardiograms refers either to the number of trips completed or the time interval in which they were performed. Therefore, the fact that only 57.7% of patients with "angina" showed positive tests should be weighed against two variables, (1) the possibility that the double test was not done on all cases, and (2) the uncertainty of the clinical diagnoses, since follow-up and postmortem studies were presumably not done in any of these patients.

In Group D ("No Chest Pain, Miscellaneous"), the author reports 18.2% positive cases, and suggests that this is a high incidence of "false positives". However, this group of 33 patients consists of (a) persons with "minor abnormalities in the ECG", (b) patients sent by attending physicians to "exclude heart disease" and (c) others examined for military or insurance purposes. Among 33 such patients, six (18.2%) may very well have coronary artery disease, in which event the results of the two-step test are satisfactory. Unless one is given sufficient data to prove that the patients do not have coronary artery disease, it is unreasonable to conclude that the Master test is not reliable.

The deduction that "a negative Master test does not exclude severe coronary artery disease or even impending infarction" also seems unwarranted on the basis of the evidence presented. The author cites, in support of his claim, two cases of alleged severe coronary artery disease with "negative" tests. Close examination of the reproduced tracings reveals that they are by no means negative. Case 1, in my opinion, is certainly positive, while Case 2 is probably abnormal. In Case 1, I draw your attention to lead II, taken immediately after exercise. The RS-T segment is clearly depressed somewhere between 0.5 mm. and 1 mm. In addition to the depression it has the horizontal configuration described by Mattingly *et al.*,¹⁻³ Myers and Talmers⁵ and others as "ischæmic". In Case 2, there is marked depression of the RS-T segment in lead V₄ immediately after exercise, although one would prefer a longer strip to be certain, since the base line is wandering downward. The author must either have been unaware of

these changes or of Master's criteria for positivity, since otherwise he could not have referred to both these records as "negative by Master's criteria".

Despite the statement by Dr. Horlick that "the technique as outlined by Master was faithfully adhered to", I see no indication in any of the illustrations of Cases 1 and 2 that two-minute and six-minute records were taken. Master has reported that the two-minute record is the most valuable. Again, neither is there any indication whether the tests were single or double. It is thus difficult to accept Dr. Horlick's conclusions that the "two-step" may be negative even in impending infarction, simply on the basis of two cases whose interpretation at best is questionable, and in fact probably erroneous.

In his review of the recent literature concerning the "two-step" test, the author has regrettably omitted reference to the recent work of Mattingly and coworkers,³ who pooled the resources of the Walter Reed Army Hospital, in Washington, D.C., and the Metropolitan Life Insurance Company in a study of 1000 persons of various ages followed up over an average period of seven years. The authors conclude that: (1) "The Double Standard Two-Step Exercise test is a dependable method of detecting occult coronary sclerosis." (2) "A negative response to the double two-step test excludes, for practical purposes, the presence of latent coronary insufficiency and clinically significant narrowing of the coronary arteries." (3) "The double two-step test, properly performed and properly interpreted, is of definite help in the diagnosis of coronary artery disease."

Continued research into the question of false positives is indicated, and will only be solved by studies involving long-term follow-up of a large number of persons. To this end, Dr. Master and I are currently reviewing the subsequent course of one thousand patients in our practice who have all had double "two-step" tests. We hope to be able to communicate our results in the near future.

I cannot comment on the reliability of the "two-step" in impending infarction, since under these circumstances the test is absolutely contraindicated.

125 East 72nd Street, ISADORE ROSENFELD, M.D.
New York 21, N.Y.,
February 3, 1959.

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4. MASTER, A. M., PORDY, L. AND CHESKY, K.: *J. A. M. A.*, 151: 458, 1953.
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To the Editor:

My study was a retrospective one, based on an analysis of clinical charts and records. Only cases with adequate notes giving a complete history and ade-

quate description of the patient's symptoms were included. The patients were seen and examined by the house staff and by their own physicians. Complete physical examinations were recorded and relevant laboratory investigations carried out. All electrocardiograms were recorded with Sanborn Direct Writing Equipment, and Master tests were carried out in accordance with Dr. Master's criteria. Tracings were recorded immediately before exercise, and then immediately after performance of either a single or double Master two-step test, and at two, five, and ten minutes after exercise. All records were carefully scrutinized with a hand lens, and ST segment changes measured on a millimetre scale. The data on the charts were re-evaluated by the author, who was responsible for assigning the patients to one of the four categories used.

Assigned to Group A — angina pectoris — were cases fulfilling the classical clinical picture. They had pain of a constricting or squeezing type, retrosternal in location, with radiation into the arms, neck or jaws, provoked by exertion and emotional stress, and relieved by rest or nitroglycerin. Where some elements of the clinical history were equivocal or unusual, the diagnosis of possible angina — Group B — was made. Groups A and B, therefore, comprised all individuals with classical or atypical angina pectoris. Group C — chest pain, not angina — consisted of individuals with diverse chest pains which were inconstant in character, variable in location, and often associated with chest wall tenderness. They did not fulfil the usually accepted criteria for angina. No one will dispute the fact that this is a difficult group to assess, and it is here that clinical judgment and experience come largely into play. To contend that one-third of such patients "do indeed have an anginal syndrome" is a contradiction in terms, and has no basis in either clinical or pathological experience. Similarly, to contend that six out of 33 patients in Group D (no chest pain — miscellaneous) may have clinically significant coronary disease, is again a rather unlikely supposition.

It is with respect to these two groups that Dr. Rosenfeld particularly takes exception to my clinical assessment. Since we possess no independently validated method of assessing the adequacy of coronary circulation at the present time, the clinical picture must remain paramount. No one will deny that there is a considerable margin of error in clinical assessment. Until such time as a reproducible and harmless technique for quantitating coronary flow in the face of measured demand is available, it cannot be replaced. The validity of the Master standards must be considered in the light of the range of responses of so-called normals in an appropriate age range. Simonson's¹ data shown in my paper are the best available "normal" data, as far as I am aware. Even such standards are likely to be influenced by unrecognized coronary disease in the normal group. It is obvious, therefore, that so-called normal standards based on the response to exercise have little or no physiological or pathological support. If one could relate the ECG changes to such objective data as coronary flow and cardiac output responses to the exercise, then it might be possible to set up valid electrocardiographic criteria.

With reference to the cases illustrated in my article, Dr. Rosenfeld states that the post-exercise record in Case 1 is clearly abnormal. I have carefully restudied

the original tracing, using a hand lens. In lead 2, resting, the ST segment is depressed 0.1 to 0.2 mm. and has a plane configuration. After exercise the ST segment depression is not greater than 0.4 mm., and is in fact less plane than it was in the resting state. It cannot, therefore, be considered as positive by Master's own criteria. In only one of the three beats shown was the ST segment depressed more than 0.4 mm. However, in this beat the PQ segment slopes downward, and projection of the PQ to meet the ST revealed that the ST segment is not unduly depressed.

With respect to the ECG in Case 2, Dr. Rosenfeld has again failed to note the downward sloping PQ segment, which results in a false impression of the ST segment. I would refer him to Lepeschkin's² excellent article on this point. In both cases, the subjects completed the Master's double test in three minutes, and electrocardiograms were recorded as usual, at rest, immediately after exercise, and two, five, and ten minutes after exercise. The number of single and double tests done in each group is shown in the accompanying table. I have also attempted to

Group	Cases	Single tests	No. positive	Double tests	No. positive
I. (Angina)	26*	14	7	9	5
II. (Possible angina)	29†	8	3	20	10
III. (Chest pain—not angina)	43	19	4	24	9
IV. (No chest pain—misc.)	32	15	2	17	4
	130	56	16	70	28

*Three patients could not complete the single test.

†One patient could not complete the single test.

show in this table the number of positive responses in the single and double tests. If we select only the subjects on whom double tests were done, and exclude the rest, we note that in Groups A and B 51.7% positive tests resulted. This compares with a figure of 54.7% with these two groups combined when all tests were included. In Group C double tests yield 37.5% positives as compared with 30.2% for the entire group. In Group D there were four positives in 17 double tests, or 23.5%. This compares with 18.2% for the entire group.

Thus, for the entire group under study—131 individuals—there were 69 with double tests, or little better than half. In none of the groups was there much difference when those with single or double tests were compared. It must be remembered, however, that single or double tests were selected after consideration of the subject's symptoms.

I regret that I was unaware of the excellent article by Robb, Marks and Mattingly³ in which careful follow-up tests were carried out on subjects who had been studied with Master's test. The last paragraph in their paper deserves to be quoted in its entirety:

"The results of the follow-up study of the Walter Reed Hospital indicate that Master's criteria for an abnormal response, especially isolated T-wave change and transitory junctional S-T depression, are too inclusive and their usage results in the overdiagnosis of coronary disease. There is some indication of this in the experience on life insurance applicants also.

Moreover, in studies of normal groups which have been followed up for extended periods of time, an abnormal response by Master's criteria has been reported in as high as 25% of the cases studied. These findings indicate that use of Master's criteria produce a large percentage of false positives, and accordingly, all of his criteria cannot be considered reliable in the detection of coronary disease. The most valid is S-T segment depression of ischemic character which exceeds 0.5 mm."

I see no serious conflict of opinion between the views expressed in my paper and those noted above.

L. HORLICK, M.D., F.R.C.P.[C]

Department of Medicine,
University of Saskatchewan,
University Hospital, Saskatoon,
February 23, 1959.

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VITAMIN C FORTIFIED MILK

To the Editor:

We have read with some interest the short communication of Dr. Harry Medovy on a plea for the fortification of evaporated milk with vitamin C, which appeared in the February 1 issue of the *Canadian Medical Association Journal*.

Dr. Medovy has well pointed out the reasons why orange juice is frequently omitted from the diet of infants in his area and in the Toronto area. Certainly the addition of vitamin C to evaporated milk would overcome this problem, if the infant, the child, and even the adult, were always sure to be fed evaporated milk fortified with vitamin C.

If vitamin C were added to evaporated milk and the product marketed as a "milk," mothers would raise their children for at least one year without the addition of citrus juices to the diet. Is it proposed that these children continue to drink only evaporated milk, or that the education of the mother and child about natural dietary sources be postponed until after the first year when the mother and child rarely visit the doctor? The first year presents the greatest opportunity to teach permanent good food habits to the mother and her child; in this particular instance, that attention must be paid to adequate dietary provision of vitamin C throughout life. If we are to become so effete that we are unable to teach the mothers of our own country good food habits and get them to follow them, then it would appear that we are neglecting our duties.

Further, is it Dr. Medovy's proposal that all evaporated milk sold in Canada be fortified with vitamin C by law? If not, what is there to ensure that many mothers will distinguish between the evaporated milks that are fortified and those that are not; indeed, that they will realize that any other milk is not an adequate source of vitamin C. The general population might well come to feel that any milk contains adequate amounts of vitamins C and D.

If certain infants do not take citrus juices healthily or well, would it not be wise to substitute vitamin C fortified apple juice or to recommend the fortification of tomato juice for this purpose? Both of these are native products and in the original fresh state can serve as important sources of vitamin C in the ordinary diet of the child and adult.

There may be a place for evaporated milk fortified with vitamin C in the feeding of certain infants and elderly people. Would it not be wiser, however, to label such a preparation as a "special formula?" This would encourage the mother to use it only on the advice of her physician and would make his job of nutrition education easier.

Although it is unlikely that an excessive intake of vitamin C would cause harm, an excessive intake of vitamin A may cause periostitis; an excessive intake of vitamin D is believed to cause failure of infants to gain and prosper, with renal calcification. There is some suggestion that harmfully excessive intakes of vitamin D by infants have resulted from the widespread fortification of foods with this vitamin in some countries.

There are dangers as well as benefits from the fortification of natural foods. The present suggestion may have merit as a "special formula" to be used in special cases at the physician's discretion. It should not be allowed, however, to confuse the population about the nutritional qualities of milk in general, which are excellent but do not provide a sole source of vitamin C, or to reduce the impetus for training in good food habits at an early age.

J. C. RATHBUN, M.D.
J. A. F. STEVENSON, M.D.

Department of Pædiatrics,
The University of Western Ontario,
392 South Street,
London, Ont.,
February 9, 1959.

To the Editor:

I welcome the opportunity to reply to Professor Rathbun's letter in regard to my communication on vitamin C fortified evaporated milk.

Dr. Rathbun's letter agrees completely with the main point of the communication, namely, that scurvy would be eliminated if all babies were fed vitamin C fortified evaporated milk in infancy. It remains only to point out that those infants fortunate enough to be breast-fed would not require this insurance.

Professor Rathbun raises two questions:

1. Would not the adoption of vitamin C fortified evaporated milk mean the postponement for a year or indefinitely of anticipatory guidance of the mother in matters of nutrition?

2. Would there be a danger of excessive vitamin intake resulting from the use of vitamin fortified foods?

As regards the first question, there is certainly no desire on our part to interfere in any way whatsoever with the education of the mother in proper nutritional habits. There is no reason why the general acceptance of vitamin C fortified evaporated milk should lead to a decline in enthusiasm on the part of the medical profession for anticipatory guidance of the mother in matters of nutrition. We have had vitamin D fortified

evaporated milk with us for many years, and certainly this has not eliminated the desire or enthusiasm of the physician to instruct mothers in the importance of correct feeding of their babies. The further addition of vitamin C is not likely to make any difference. Mothers continue to use vitamin concentrates now, although most of them use vitamin D fortified milk for their babies. There is no good reason why citrus fruits could not be used along with the vitamin C fortified milk.

The second question should be considered apart altogether from the problem of scurvy and its prevention. Although there is no known danger from overdosage with vitamin C, there is danger in excessive intake of vitamin A and D, as Professor Rathbun has pointed out. Because evaporated milks now contain 800 i.u. instead of the former 400 i.u. of vitamin D per reconstituted quart, the further addition of vitamin A and D through the medium of multiple vitamin concentrates may possibly provide the infant with more of these vitamins than is desirable. The whole matter of vitamin supplements and vitamin fortified food products needs to be reviewed in order to guard against the danger of overdosage. With this, we are in complete agreement with Professor Rathbun.

Our argument was simply that scurvy can be prevented among the young and the old, the intelligent and the less intelligent, and particularly among those to whom the teaching of good nutritional habits does not penetrate and for whom natural dietary sources of vitamin C may not be available because of geographic or economic considerations.

University of Manitoba,
Children's Hospital,
Winnipeg 3, Man.,
February 19, 1959.

HARRY MEDOVY, M.D.,
Professor and Head,
Department of Pædiatrics.

"MAPLE SUGAR URINE DISEASE"

To the Editor:

See pages 90, 91 and 104 of the *British Medical Journal* of January 10, 1959.

I have not been a Canadian long enough (and sugar maples don't grow in Newfoundland) to work up sufficient indignation over the above articles to deal with the subject adequately.

The idea of naming a disease after your—or I should now say "our"—tree which produces our national emblem is outrageous, and one of the articles says "odour of maple syrup or burnt sugar", which adds insult to injury.

Again, how vastly wider is the ability to recognize the odours of burnt sugar than that to recognize maple syrup, so why not have called it "caramel urine disease"?

If ever there was a case for naming a disease after its discoverer, surely here it is, and it is not even suggested that there is any connection between the disease and the ingestion of maple syrup. When I saw the title "Maple Sugar Urine Disease" I at once thought there must be some special form of diabetes connected with maple sugar.

*See also Editorial Comment, page 467.

Here is something for our P.R.O. to get busy with; and also the subject could give rise to the odd quip in after-dinner speeches at our Joint Meeting in Edinburgh.

CLUNY MACPHERSON, M.D., C.M.

65 Rennie's Mill Road,
St. John's, Nfld.,
February 4, 1959.

OBITUARIES

DR. J. C. GILLIE, 72, a past President of the Ontario Medical Association, died in the McKellar General Hospital, Fort William, Ont., on January 7. Born in North Bay, Ont., Dr. Gillie moved to Fort William in 1912 after graduating from Queen's University. He was an executive member of the Thunder Bay Medical Society and did a great deal of work for the modernization and expansion of the McKellar General Hospital. A council member of The College of Physicians and Surgeons of Ontario, he served as Vice-president in 1956-57. Last year, at the Annual Meeting in Halifax, Dr. Gillie was made a life member of the Canadian Medical Association.

He is survived by his widow.

DR. J. A. MacPHEE, 74, died on January 23 at the Prince County Hospital, P.E.I. He had been in ill health for some time. Born in Charlottetown, Dr. MacPhee taught school for a few years before going to McGill University, where he graduated in 1910. During the First World War he went overseas with the Royal Canadian Medical Corps and was discharged with the rank of Captain. In World War II he was commanding officer of a military hospital at Mulgrave, N.S., and attained the rank of Lieutenant-Colonel. For most of his medical career, Dr. MacPhee practised in Summerside, P.E.I. He was a life member of the Canadian Medical Association and also a past president of the P.E.I. division.

Dr. MacPhee is survived by his widow, three sons and six daughters.

DR. D. C. METCALFE, 36, died after a heart attack at his home in Windsor, Ont., on December 18. A native of Nova Scotia, Dr. Metcalfe graduated from Dalhousie University in 1948. He interned at the Saint John General Hospital in 1947 and in 1948 did postgraduate work at the Children's Hospital in Halifax. After leaving Halifax he worked in the Children's Memorial Hospital in Montreal and then served for three years in the Royal Canadian Air Force with the rank of Squadron Leader. On his discharge from the Air Force, Dr. Metcalfe practised as a paediatrician in Windsor. He also served as medical officer for the Chrysler Corporation.

He is survived by his widow and three sons.

DR. MERVYN D. UPTON, 50, died at his home in London, Ont., on December 31. A native of London, he was educated at the University of Western Ontario Medical School. After graduating in 1933, Dr. Upton interned at the Victoria Hospital and in 1935 started his private practice.

PROVINCIAL NEWS

BRITISH COLUMBIA

In the Speech from the Throne, an important feature, from the medical point of view, was the announcement that in future mental health services will be placed under the Ministry of Health, which will be a separate portfolio. Hitherto the Hon. Eric Martin has been Minister of Health and Welfare — and it is felt that there will have to be two ministers, one for health and one for welfare. There will be greater provision for mental health services and services for retarded children, etc.

Dr. Stewart Murray, City Medical Health Officer for Vancouver, told the Metropolitan Health Committee that no cases of diphtheria or typhoid occurred in Vancouver in 1958, and only three cases of poliomyelitis. He opposed any suggestion of opening recreational areas in the city watershed, as suggested by some eager seekers after recreation, on account of the danger of typhoid.

Gamma globulin for inoculation against measles will soon be available free of charge to small children (under four, or older if sickly) and to women in early stages of pregnancy. They will get this through their family doctors.

Nurses in eight lower mainland hospitals are greatly upset over their failure to obtain a monthly increase of \$20 unanimously recommended by a conciliation board.

The hospitals are all in favour of granting the increase but hesitate to do so, as the Hon. Eric Martin, Minister of Health and Welfare, will not guarantee that the Government, through the British Columbia Hospital Insurance Service, will pay any more to provide this increase, and has informed all hospitals that they should not budget for higher expenditures in 1959 until they have been told what funds are available.

Nurses are seriously considering taking strike action if they do not obtain what they regard as their just due.

By the will of Mrs. G. F. Laing of Vancouver, a bequest of \$50,000 was left to the British Columbia Cancer Society.

The research facilities of the British Columbia Medical Research Institute will be merged with the research departments of the University of British Columbia. A laboratory will be built on the top floor of the medical school building at the Vancouver General Hospital and will be known as the G. F. Strong Laboratory for Medical Research, with Dr. Kenneth Evelyn in charge as Director.

The British Columbia Medical Research Institute, which has given \$95,000 to the University of British Columbia Development Fund, will donate its research equipment, valued at \$61,000, to the new laboratory; it will continue to operate and will act to raise money for medical research in British Columbia.

J. H. MACDERMOT

ALBERTA

The Fifth Annual Scientific Meeting of the Alberta Chapter of the College of General Practice, associated with the meeting of the Section of General Practice of the C.M.A., Alberta Division, was held at Banff from January 28 to 30. These meetings are becoming increasingly popular and the attendance increases yearly. Apart from formal talks, workshops were held in the various branches of medical practice, a panel of three experts leading the discussions. This type of presentation was considered very valuable. The featured speaker at the meeting was Dr. R. O. Brandenburg of Rochester, Minnesota, an internist at the Mayo Clinic. The remaining speakers came from the University of Alberta and from Calgary and Edmonton.

One evening meeting was given over to business, and elections were held with the following results: College of General Practice (Medicine), Alberta Chapter: President, Dr. R. Woolstencroft, Calgary; Secretary, Dr. Noel Smith, Calgary; Treasurer, Dr. Tom Saunders, Calgary. For the Section of General Practice, C.M.A., Alberta Division, the following were elected: President, Dr. John A. Weddell, Red Deer; Secretary, Dr. Jack C. Staples, Red Deer; Treasurer, Dr. Bob Zender of Stettler.

The social arrangements of the meeting were excellent, and the ladies were invited to all noon luncheons. Banff was chosen as the venue for next year's meeting.

(A commentary on the state of culture in Alberta was the fact that at the Annual Ball, when the orchestra stepped down for a rest, a nine-piece orchestra was recruited from the doctors present, with Dr. Brandenburg joining in and excelling on the clarinet.)

The National Cancer Institute of Canada has awarded a grant to Dr. Walter C. MacKenzie, director of the department of surgery at the University of Alberta, to assist in chemotherapy investigations. These investigations constitute part of the "Chemotherapy adjuvant therapy program" as outlined by the National Institute of Health at Bethesda, Maryland. The Alberta group will investigate the clinical effects of nitrogen mustard and Thiotepea on carcinoma of the stomach, colon, anus and lung.

Figures recently released by the Alberta Tuberculosis Association indicate that 176,000 citizens received chest x-ray examinations during 1958. Apart from 15,000 examinations which were made in the Calgary and Edmonton Clinics, these examinations were carried out by the two mobile x-ray units which the Association turned over to the Provincial Department of Health, Tuberculosis Division. Cost of the operation of the unit is split equally between the A. T. A. and the Provincial Department of Health. The A. T. A. derives its funds exclusively from the sale of Christmas seals. This year's receipts are expected to be in the neighbourhood of \$225,000.

The results of these examinations are not complete, but the preliminary figures indicate that 471 probable tuberculosis cases were discovered in the survey. The incidence of tuberculosis was found to be much higher in the northern half of the province, probably because of the lower standards of living in isolated areas, particularly among the Metis population.

The officers of the Edmonton Academy of Medicine have been installed with: Dr. Hal Richard, President; Dr. Sam Hanson, First Vice-President; Dr. B. M. Wheeler, Second Vice-President. Dr. W. S. Anderson is Secretary; Dr. Andrew Cairns is Treasurer; and the Executive are: Drs. Max Dolgoy, Charles Learmonth and R. Francis.

In Calgary, the Calgary and District Medical Society has a new executive made up of: President, Dr. M. D. Mitchell; Vice-President, Dr. Lorne Mitchell; Secretary, Dr. H. C. Worrall; Treasurer, Dr. A. V. Follett; Librarian, Dr. R. P. Douglas.

Final approval for demolition of the old Calgary General Hospital, which has been standing virtually empty since the new building was occupied, has finally been given and plans are now going forward for construction on this site of a 150-200 bed active convalescent wing. So far plans are in the hands of the architect and only the demolition contracts have been let.

W. B. PARSONS

ONTARIO

The Plummer Memorial Public Hospital, Sault Ste. Marie, has received a federal health grant of \$78,146 towards construction of a nurses' residence and training school.

St. Michael's Hospital, Toronto, has been granted \$24,920 to assist in the cost of renovating teaching facilities and patient area.

The Women's Auxiliary of the Toronto General Hospital donated \$18,500 to the hospital this year; \$3000 of this is for clinical investigation.

Dr. P. J. Moloney, Connaught Medical Research Laboratories, addressed the Toronto Diabetes Association on "Antibodies to insulin".

The Salvation Army has opened a new Grace Hospital in Toronto; costing \$2,500,000, it will replace the old building opened in 1906 and enlarged in 1925. The new building has six floors with 125 adult beds and 88 infant cots. Provision has been made for the care of 40 gynaecological and surgical cases. Out-patient facilities include a playroom for children.

Grace Hospital is for women only and takes care of many social service cases. Its facilities are open to all; everyone is asked to pay her bill, but the Army excuses poor people and never sues for payment. The rate set by the Hospital Services Commission is \$19.95 a day.

A public hospital to care for chronically ill elderly citizens will be built in Toronto. Plans have been prepared for a \$4,685,000, seven-storey building with 632 beds at the site of the present Riverdale Hospital. Plans provide for a large therapy pool and occupational therapy workshops. Accommodation will be in two-bed and four-bed wards. The design is a cross between a home for the aged and an active treatment general public hospital.

Construction beginning in October will require 18 months for completion. The Ontario Hospital Commission has set a rate of \$16 for public ward care and \$22 for semi-private accommodation.

Dr. Dmytro Buchnea of the Banting and Best Department of Medical Research, University of Toronto, has received a Glycerine Research Award for 1958, a scroll and a \$300 prize for his synthesis of phosphatides. Dr. Buchnea was associated in this work with Dr. Eric Baer, who received the same award in 1953. Both men work in the subdepartment of synthetic chemistry. This is the first time recognition has been given twice to the same laboratory for accomplishments in this field. LILLIAN A. CHASE

A series of special courses has been arranged under the direction of the Division of Postgraduate Medical Education, University of Toronto. The first, a symposium on low back pain, was given at Sunnybrook Hospital on January 16 and 17. The second, a course in public health and preventive medicine ("Health Supervision of Children") was given February 9-11 at the School of Hygiene. The third, a course on fractures and trauma, is scheduled for March 16-21 at the Toronto General Hospital.

KINGSTON NEWS

Opening of the New Etherington Hall, Queen's University

"Completion of Etherington Hall — named after the late Dr. Frederick Etherington — was an important milestone in the history of the Faculty of Medicine at Queen's University," said Principal W. A. Mackintosh in an address at the unveiling of a plaque in Dr. Etherington's memory on February 7, 1959.

Dr. Mackintosh spoke of the years of planning with many frustrations and disappointments that had preceded the completion of this building on property owned by the Kingston General Hospital. He paid tribute to the campaign for funds carried out under the chairmanship of Dr. Ford Connell and Dr. Ettinger among the medical alumni. He praised the patience and fortitude of Dean Ettinger, who had managed to bring together the desires and demands of the members of the medical staff of the University in a most statesman-like manner. He recalled Dr. Etherington as an anatomy teacher, who as he remembers made pertinent remarks on many activities, much to the delight of the students. He also spoke of Etherington's interests in golf, Shakespeare, drama and boxing. He referred to him as a personality who was robust, poignant, laconic and an expert in sharp comment, who assumed a sardonic mood to mask great human ideals of generous loyalty and who preferred deeds to words.

Dr. Ettinger recalled that Dr. Etherington graduated in 1902, became a lecturer in anatomy in 1905 and was the first professor in anatomy in 1907. He practised surgery after 1911, and during the First World War he was colonel-in-charge of No. 5 Stationary Hospital in Kingston and later commanded No. 7 Canadian General Hospital, staffed from Queen's, in France. He was Dean of Queen's Faculty of Medicine from 1929 to 1944, and his many offices included Presidency of the Medical Council of Canada and of the Ontario College of Physicians and Surgeons.

A large Union Jack, which had flown over his hospital in France, was drawn back by Dr. Ettinger, unveiling the bronze plaque which reads as follows: "This building is named for Frederick Etherington,

C.M.G., M.D., LL.D., 1878-1955, anatomist, surgeon, soldier, dean of medicine, laconic in speech, swift in decision, benefactor, and for 38 years a loyal servant to this university." R. C. BURR

QUEBEC

Plans are almost complete for the next Annual Meeting of our Division. This will be held at Chicoutimi on May 7 to 9. An outstanding scientific program has been drawn up by the Program Committee, under the chairmanship of Dr. S. Arthur MacDonald, while Dr. Sylvio Leblond, our President-Elect, is seeing to it that the social aspects will surpass anything that we have had before. As in previous meetings, we will again have interesting and instructive scientific and commercial exhibits.

The Rehabilitation Institute of Montreal, which has achieved wide acclaim for the work done, will soon have its own home. A new 111-bed six-storey hospital will be built for the Institute on Darlington Ave. The building is expected to be ready by the fall of 1960. The hospital will have many unique features and appliances, all forming a vital part of skilled efforts to help the disabled. The work by the Institute has already shown that many patients hitherto regarded as incurable can be restored to useful lives. The new plant will greatly extend this service.

The Faculty of Law of McGill University provides each year a series of extension lectures and panel discussions for members of the Bar. This year it was decided to air the doctor's role in the courtroom, and for this reason physicians and hospital administrators were invited to attend. The series was opened on Monday evening, February 2, by Dean W. C. J. Meredith, who spoke on medical evidence in civil cases. His talk was preceded by the showing of the film "The Defendant Doctor". On February 9, Mr. Justice Claude Prévost presided over a panel discussion on medical evidence in criminal cases with Joseph Cohen, Q.C., and Dr. Jean-Marie Roussel, medico-legal expert, as participants. The last session was held on February 16 with Mr. Justice George S. Chailles presiding and panel members Dr. J. Gordon Petrie, Dr. Antonio Samson and Dr. Jean Saucier. They discussed some of the medico-legal aspects of trauma. There is growing recognition of the importance of medical evidence in civil and criminal cases. This series was therefore most timely as well as instructive for those fortunate enough to participate in them.

Dr. Herbert E. Coe of Seattle, Washington, delivered this year's Cushing Memorial Lecture at McGill University on January 30. He emphasized that the specialty of child surgery arose less than half a century ago because the methods of general surgery produced poor results when applied to paediatric surgery. The lives of many infants who die from congenital disorders could now be saved if more children's surgery was taught in medical schools. Conditions once thought hopeless can be cured if the special delicate techniques needed in operations on children are studied and applied by general surgeons. This famed 77-year-old surgeon showed throughout his talk the enthusiasm of a novice.

A refresher course for French-speaking physicians was held from February 2 to 5 at the Hôtel-Dieu Hospital in Montreal. Seventy-five physicians from Quebec and Ontario attended the course, which was primarily devoted to the study of medical problems commonly encountered in general practice. Some 60 senior staff men presented an excellent program which included formal lectures, panel discussions and clinical sessions. The course ended with a banquet at the Hélène de Champlain Restaurant in the evening of the last day.

A safe and powerful new x-ray apparatus through which radiologists can watch bright moving pictures of the heart, respiratory system and other internal organs was demonstrated recently at Laval Hospital, in Quebec City. Developed by Philips of Eindhoven, Holland, the \$100,000 installation is the first of its kind in Canada. Advances incorporated into it include two electronic units, which intensify the brightness of ordinary fluoroscopic x-ray pictures 1000 times, and a built-in mirror cine-camera for recording the action of internal organs on 35-mm. film. The intensifying unit permits radiologists to prolong their examinations without subjecting themselves or their patients to excessive radiation. The camera, which has a variable speed control, will give slow motion pictures of rapid and complicated actions like those of the speech organs. The operation of this equipment is supervised by the director of the hospital, Dr. Alphonse L'Espérance. The new apparatus will be invaluable for medical research, instructing students and observing the action and speed of movement of internal organs.

The opening meeting of La Société Médicale de Montréal was held on January 20 at Hôtel-Dieu Hospital. Invitations had also been extended to all members of the Montreal Medico-Chirurgical Society, and thereby members of both societies were given the opportunity to hear an excellent presentation by Dr. D. L. C. Bingham, professor of surgery at Queen's University, Kingston. The title of his talk was "Carcinoma of the lung".

The last Society evening of the Montreal Medico-Chirurgical Society was on February 2. It began with a buffet supper, followed by a symposium on "Evaluation of symptoms commonly observed in office practice". The moderator Dr. John J. Howlett presented to members of the panel in sequence six common complaints observed in office practice and asked particular members to discuss these. The panel members were Drs. W. J. McNally, H. S. Mitchell, W. F. T. Tatlow, A. MacLeod and Alan G. Thompson. Invitations to this meeting had also been extended to all members of La Société Médicale de Montréal, and the auditorium at the Montreal General Hospital was filled to capacity.

Dr. Francis L. McNaughton of the Montreal Neurological Institute has been promoted from associate professor to professor of neurology at McGill University. He has been a member of the staff of the Institute since 1935 and has been intimately associated with the research and treatment activities of the Institute, whose director is Dr. Wilder Penfield.

A. H. NEUFELD

NEW BRUNSWICK

The Royal College of Physicians and Surgeons of Canada has recently granted the F.R.C.S. (Surgery) to Dr. Robert Dysart and the F.R.C.S. (Obstetrics and Gynaecology) to Dr. Victor D. McLaughlin. Dr. Paul A. Pugh has received certification in obstetrics and gynaecology from the Royal College. All of these doctors are practising in Moncton, N.B.

Dr. Georges Grondin has begun the practice of surgery and Dr. Egbert Daigle is specializing in anaesthesia in Moncton.

Dr. James Corston of the Department of Obstetrics and Gynaecology, Dalhousie University, visited the North Shore Medical Society at Bathurst on January 27, and spoke at afternoon and evening meetings on antepartum haemorrhage and made observations on induction of labour, twins, and diabetes in pregnancy. This meeting was sponsored by the N.B. Chapter, College of General Practice of Canada.

At Fredericton, on January 29, Dr. John O. Godden, Associate Professor of Preventive Medicine, Dalhousie University, addressed the doctors of southern New Brunswick on jaundice, and the following afternoon and evening Dr. Godden discussed the same subject at St. Stephen, where doctors from nearby centres in the State of Maine joined their colleagues of the St. Croix Medical Society. Refreshment and dinner are not unusual additions to these medical meetings, but at St. Stephen, that hospitable town, the doctors' wives were entertained by Dr. and Mrs. Brownrigg.

The Moncton Tuberculosis Hospital will be closed, probably in April. The patients remaining in its wards at present will be transferred to the four other sanatoria in the province. Improved methods of treatment of tuberculosis by surgery and new drugs have reduced the number of beds required in New Brunswick, as in other areas.

The New Brunswick Department of Health is happy to state that only three cases of paralytic poliomyelitis were reported in the province in 1958. None of these three persons had been vaccinated. It is believed that the small number of cases is due to the intensive program of vaccination with Salk vaccine made available to children up to Grade XII, provided free of cost; as elsewhere, it is almost routine to vaccinate infants against this disease in their first year after their triple toxoid inoculations.

Dr. Carl Trask, Director of the Saint John General Hospital, attended the meeting of the Society of Medical Administrators at San Juan, Puerto Rico, in late January.

A. S. KIRKLAND

BOOK REVIEWS

HISTORY OF THE CANADIAN MEDICAL ASSOCIATION, Volume II. H. E. MacDermot, 153 pp. Illust. The Canadian Medical Association, Toronto, 1958. \$2.50.

It has been stated that he who is unwilling to learn the lessons of history must be prepared to relive it. This admonition applies to organizations as well as to individuals, and the appearance of Volume II of the *History of The Canadian Medical Association* provides us all with the opportunity to learn from our recent past. Dr. H. E. MacDermot has sketched the record of The Association from 1922 to 1956, the period of our greatest growth and activity. It is no mere coincidence that these years constitute, substantially, the Routley Era and the record of accomplishment owes much to the work of the man who served, for over 30 years, with distinction in the appointment of General Secretary.

Dr. MacDermot applies a broad brush to his canvas and provides us with accurate and interesting accounts of such varied topics as hospital services, health insurance, the origin of the Royal College of Physicians and Surgeons of Canada and the College of General Practice of Canada, international medical organizations and the highlights of our own Annual Meetings. Members whose professional lifetimes encompass the period in question will find themselves reminded of many developments in which they participated, and newcomers to the profession will be informed of the devoted work of their predecessors.

Volume I of our *History* (1867-1921) was published in 1935 and is, unfortunately, out of print and unavailable. This too was written by Dr. Ernest MacDermot, who since putting down the editorial pen has resumed that of the official historian. Fortunate, indeed, is The Association to have enjoyed the services of a man whose energy and aptitude make it possible for us to see so clearly the way we have come. It will interest members to know that Dr. MacDermot's current task is to prepare the outline for a volume "One Hundred Years in Canadian Medicine" to mark our centenary eight years hence.

Volume II of the *History of The Canadian Medical Association* is recommended reading for every Canadian doctor. After whetting his historical appetite, he will be impelled to beg, borrow or steal one of the rare copies of Volume I.

SUBARACHNOID HÆMORRHAGE. John N. Walton, Durham University. 350 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1956. \$5.00.

This excellent monograph on subarachnoid hæmorrhage is based on the author's personal survey of the clinical and pathological material from 312 cases studied in Newcastle-on-Tyne. The survey, as Sir Charles Symonds says in his foreword, is "both comprehensive and detailed, without anything of importance being omitted".

The pathological section is particularly well done, and illustrates the fact that with aneurysms we are not simply dealing with hæmorrhage into the subarachnoid space; we are dealing with a bleeding point that may result in intracerebral extension, subdural extension, or alteration in the calibre of the vessel on which the aneurysm lies, with resultant ischæmic in-

farcion of the brain. As pointed out by the author, the area of infarction is not necessarily within the distribution of the vessel on which the aneurysm lies. The role of spasm is discussed.

The chapter on prognosis would have been improved had the author's aneurysm material been broken down to indicate the prognosis in the varying sites of origin of the aneurysms from the circle of Willis. On the whole, this is not a serious criticism, considering the wealth of material that is available in the monograph.

The author's own material is discussed in conjunction with nearly all the important literature available on this subject. This feature, coupled with the inclusion in the work of a very extensive bibliography, makes it an important source of reference for this entire subject. This monograph is assured of a place in the library of everyone interested in the pathological and clinical disorders of the central nervous system.

A PRIMER ON COMMON FUNCTIONAL DISORDERS. J. W. Fleming. 174 pp. Illust. Little, Brown and Company, Boston and Toronto, 1958. \$5.00.

The material presented in this book is an account of the problems in the diagnosis and management of functional disorders. The author gives a brief and clear account of his views, and these should be of assistance to physicians who have to deal with general functional disorders. While he mainly discusses the psychological aspects of medicine, the author emphasizes that organic disease and functional illness are often interrelated. It is with these aspects, together with general functional disorders, that he is concerned. He points out that major psychiatric illness should be managed by a psychiatrist, and for this reason does not deal with these problems.

The disorders dealt with include the hyperventilation syndrome, headache, the gastric acidity syndrome and peptic ulcer, irritable gastro-intestinal tract, obesity or overeating syndrome, allergy headaches, and gynaecological syndromes. Although there are points about which one can differ with the author concerning his approach to these problems, the general aspects are fairly presented. This book can be recommended as a good general account of these problems and how to manage them. It should be of value to busy physicians wishing to refresh their knowledge.

PARENT-CHILD TENSIONS. Berthold Eric Schwarz and Bartholomew A. Ruggieri. 238 pp. J. B. Lippincott Company, Philadelphia and Montreal, 1958. \$4.95.

This book, which is written by a pædiatrician and a psychiatrist, attempts to present and clarify some of the problems which arise in the parent-child relationship. It describes many of the common disturbances which arise in children when this relationship is not ideal. The focus for the most part is on behaviour problems and, according to the preface, it is the intention of the authors to reach a wide audience and present their material in a non-technical and readable style. These objectives are reasonably well achieved.

It is very difficult to assess a book of this kind because it is neither quite popular nor quite scientific. It is recognized that the authors have undertaken a very difficult task, and it remains to be seen whether they have achieved their stated objective of helping parents to understand some of the problems with which they are faced.

UROLOGY IN GENERAL PRACTICE. F. C. Hamm and S. R. Weinberg, State University of New York Downstate Medical Center, New York. 293 pp. Illust. J. B. Lippincott Company, Philadelphia and Montreal, 1958. \$6.00.

The material in this book is being used to teach medical students at the Medical Center of the State University of New York. It does not pretend to be a complete work in urology, but as a primer it can be classified as excellent. The material is presented in a simple and straightforward form, and the authors have avoided controversy in the presentation of their subject. They have omitted a great deal of urological mythology which has been handed down from text to text, and the book is therefore refreshingly new.

The first five chapters consist of an outline of urological terminology and methods of investigation. These are presented so as to give the reader a working knowledge of urological methods, rather than a complete review of the subject.

An interesting chapter on the role of the genitourinary system in the diagnosis of the acute abdomen is well handled. Of particular interest to the general practitioner is the differentiation from acute appendicitis. Renal physiology is presented in excellent capsule form, with particular emphasis on the end stages of renal failure and uræmia, which are so often managed by the family doctor.

Six chapters are devoted to diseases of the kidney. The subject matter is long on diagnosis and basic physiology, and short on detailed methods of treatment, which are the province of the specialist. The authors advise that all supposed renal cysts be given the benefit of surgical exploration.

A very sensible chapter on renal and urinary tract infection and antibiotic therapy is provided. The general practitioner will benefit from the review of methods for prevention of urinary calculi.

Discussion of the remainder of the urinary tract is well handled and most informative. Simple surgical procedures, such as the treatment of paraphimosis, are presented, but major surgery is not detailed. A rational basis for early orchidopexy at five years of age is presented, and the authors are impressed by the increased incidence of carcinoma in undescended testicles. The references are adequate, and the illustrations illuminating.

From the viewpoint of the general practitioner, this book is an excellent review of the current practice of urology.

LABORATORY MEDICINE—HEMATOLOGY. John B. Miale, University of Miami School of Medicine, Miami, Fla. 735 pp. Illust. The C. V. Mosby Co., St. Louis, 1958. \$13.75.

In the foreword to this book, Professor W. A. D. Anderson, the distinguished pathologist, declares that in "skillful art there is probably little difference between ancient and modern medical practice, and perhaps not too much difference between the medicine man and the physician". Although all clinicians are not expected to agree wholeheartedly with this statement, they will find it hard to quarrel with the fact that "medical research and the advances in knowledge and science of the last few decades have revolutionized the practice of medicine within a generation". This change has become obvious in the practice of hæmatology.

The present volume is the first of a series which will include one on chemical pathology and another

on microbiology. Each one is independent of the others, may be bought separately and covers each subject by itself. One of the purposes envisaged by this publication seems to be to correct or improve the relationship between laboratory and clinical medicine. The attitude of the latter towards the former may range from a complete disregard of any laboratory tests, to "covering the waterfront" with all sorts of irrelevant and expensive procedures, the interpretation of which does not cast much light on the particular problem presented by the patient. This purpose seems well achieved in this book. If the precepts enunciated therein are followed, the reader should develop "a system of thinking" (in the words of the author) which will enable him to derive full benefit from laboratory facilities at his disposal.

The traditional divisions of all hæmatology textbooks have been respected, starting with hæmopoiesis, morphology of marrow and peripheral blood, followed by erythrocytes and leukocytes in health and disease, and ending with hæmostasis. The description of the methods and procedures is contained in an appendix which occupies about one hundred pages at the end of the book.

There is an abundant bibliography at the end of every chapter which brings the reader up to 1957. The illustrations are adequate, and five colour plates are grouped together in the second chapter (morphology). They are made up of coloured photographs; most of the specimens are stained with Wright's stain. An index covers the content. The text is printed on glossy paper in clear type, and the volume is well bound in cloth.

In the experience of the reviewer, this book compares favourably with any other in this field. It has the advantage of a recent date of publication and should offer clear and useful guidance to the medical student, the clinician, the pathologist and the medical technologist.

TISSUE CULTURE. E. N. Willmer. 191 pp. Illust. Methuen & Co. Ltd., London; The Ryerson Press, Toronto, 1958. \$2.50.

This is the third edition of a well-known text on the subject of tissue culture. The demonstration of the growth of poliomyelitis virus in tissue culture opened up a whole new vista in this field and prompted the rewriting of this work. It covers culture methods, characteristics of growth, the cell colony and the medium, metabolism of growing cells, and differentiation of cell types. It is a most lucid description of this fascinating method of observing and studying cell development *in vitro*.

MEN, MOLDS, AND HISTORY. Felix Marti-Ibanez, New York Medical College. 114 pp. MD Publications, Inc., New York, 1958. \$3.00.

Dr. Marti-Ibanez is currently engaged in the publication of a number of books of essays on the history of medicine. This particular book deals with historical and philosophical aspects of antibiotics and antibiotic therapy. The ten essays reprinted in this volume have appeared separately in journals or elsewhere, and cover a very wide range of topics, not always entirely related to the title, such as "Words and research" and "On treating the whole patient".

HEMATOLOGIE CLINIQUE (Clinical Haematology). Jean Bernard and Marcel Bessis, 526 pp. Illust. Masson & Cie, Paris, 1958. 14.500 fr.

La genèse de ce livre remonte au Cinquième Congrès International d'Hématologie tenu à Paris il y a quelques années. Les nombreux tableaux préparés à cette occasion avaient été l'objet de commentaires élogieux de la part d'un grand nombre de visiteurs et les auteurs avec l'aide de 18 collaborateurs en ont tiré un des meilleurs textes d'hématologie générale publiés depuis longtemps. Ce texte fut écrit surtout pour l'usage des médecins non spécialisés bien que de nombreux hématologistes en feront leurs délices. Les auteurs se sont efforcés d'apporter toute la clarté et la précision possibles à l'exposition de cette branche de la médecine interne qui est en voie de prendre tant d'ampleur.

L'ouvrage est divisé en cinq parties qui comprennent l'hématologie générale, les maladies des érythrocytes, les maladies des leucocytes, les maladies hémorragiques et enfin, les diagnostics. De nombreux tableaux synoptiques (rappelons-nous son origine) se retrouvent à tous les chapitres. Les plus récentes découvertes, les médicaments à peine sortis du domaine expérimental, les applications des techniques les plus modernes sont mentionnés dans le texte. Les multiples observations cliniques sont puisées de la vaste expérience des auteurs. Deux innovations très louables consistent en un glossaire immuno-hématologique et un tableau de la synonymie des facteurs de coagulation. Elles attestent le souci des auteurs de dissiper toute trace de confusion. Sans se perdre dans les détails techniques, on trouve au chapitre de la fonction hémostatique une explication claire et succincte des principales épreuves de l'hémostase.

La présentation de l'ouvrage, comme celle de la plupart des publications de la maison Masson, est très soignée. Ce fort volume contient 295 figures dont plusieurs sont la reproduction de photographies obtenues par le microscope électronique et d'autres par le microscope de phase. Les 37 planches en couleurs montrent très fidèlement l'apparence de frottis colorés au Giemsa. Le papier est de bonne qualité et plusieurs feuillets sont de papier glacé.

Au train où vont les choses, ce livre sera peut-être largement dépassé d'ici quelques années, ce qui est d'ailleurs le sort de la plupart des textes médicaux, mais à l'heure présente il forme la meilleure vue d'ensemble des connaissances actuelles en hématologie. Par sa présentation didactique et son orientation clinique, ce livre devrait s'assurer une large diffusion et une place de choix dans les bibliothèques médicales et surtout dans celle du médecin praticien et celle de l'étudiant qui prépare les examens supérieurs.

DAS BLUTEIWEISSBILD: DIAGNOSE UND THERAPIE DER BLUTEIWEISSSTORUNGEN (The Blood Protein: Diagnosis and Therapy of Blood Protein Disturbances). Rolf Emmrich, Magdeburg. 227 pp. Illust. 2nd ed. Ferdinand Enke Verlag, Stuttgart, West Germany, 1957. DM 40.

The author's intention in writing this brief but comprehensive discussion of blood proteins and their disturbances is to present material for the general practitioner and internist without special knowledge of techniques of blood protein analysis. It is therefore a simplified version of the material contained in such large textbooks as that of Wuhrmann and Wunderly. The book begins with a consideration of the blood protein fractions and their significance in clinical diagnosis. Various

techniques are then explained in sufficient detail for the non-specialist in these methods. The various protein reactions such as the Takata, the zinc sulfate, and the thymol turbidity test, are included. The book continues with a brief survey of the formation and metabolism of blood proteins, and a description of the disturbances in the blood protein picture. The significance of the latter in differential diagnosis and in prognosis is then discussed, and the book ends with a consideration of treatment of disease with blood proteins (for instance, by plasma and serum infusion) and treatment of disturbances of the latter. The book is well illustrated and provided with a bibliography.

THE ORGANIC PSYCHOSES. A Guide to Diagnosis. J. G. Dewan and W. B. Spaulding, University of Toronto. 170 pp. Illust. The University of Toronto Press, 1958. \$5.95.

The authors have written a modest book, which is very refreshing in these days. It is modest in tone, not in significance, because packed into these few pages is a wealth of material, simply (aside from the vocabulary, which is necessarily cumbersome), lucidly and pleasantly presented.

The etiological chart at the beginning is a masterpiece of succinct and systematic thinking. The following chapters deal with each item in a workmanlike manner. Particularly well done are the discussions on metabolic disorders and dementia. One would have liked to read a little more on the exogenous intoxications. The choice of the brief but adequate case histories is particularly enlightening.

The book will be particularly useful to those whose field is not essentially psychiatric. There is so much emphasis today upon the psychogenic aspect of mental illness that a book which indicates the prevalence of organic bases is most useful. As a refresher to practitioners in this field, it is outstanding. It should be especially useful to the clinical psychologist, whose efforts might be more effective if the organic contribution were more adequately recognized.

The authors start with the fundamental thesis that "the brain is affected in every organic psychosis . . ." and proceed to show how the localized affected area may be identified. Every well-known test is mentioned, and some more esoteric and not so widely used. Proper emphasis is given to the use of mental tests in relevant situations.

One suggestion comes to mind. A short glossary should be included (in the next edition) for those working in adjacent areas. Altogether, this is an excellent contribution to an important field of medical practice.

BACTERIAL AND MYCOTIC INFECTIONS OF MAN. Edited by René J. Dubos, The Rockefeller Institute, New York. 820 pp. Illust. 3rd ed. J. B. Lippincott Company, Philadelphia and Montreal, 1958. \$8.50.

This is the third edition in 10 years of this invaluable textbook of bacteriology. It should be recalled that this volume is a result of the co-operative efforts of many contributors, each being an expert in his own field. The problems of host-parasite relationship and the principles of antimicrobial therapy are particularly well presented. This text is an excellent reference for the medical student and general practitioner and fills the gap between the ordinary textbook of bacteriology and the standard textbook of medicine.

LEHRBUCH DER CHIRURGIE (Textbook of Surgery). M. Allgoewer. Edited by H. Hellner and others. 1112 pp. Illust. 2nd ed. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1958. \$20.00.

The second edition of this surgical textbook soon followed the first—undoubtedly a sign of success. It is written by 33 representatives of German surgical schools and is well edited, with not more than the unavoidable overlapping.

Following the modern trend, patho-physiology is usefully emphasized but not to the neglect of anatomical essentials. The different chapters are introduced by short historical reviews. Diagnostic methods and therapeutic indications are clearly expounded and references are made to very recent work. The general presentation of tumours, with a short addition on radioactive isotopes in surgery, is very readable and concise, and contains material not often found in books of similar scope. The chapters on the surgical diseases of the chest, heart, and vascular systems—these new and fast-changing fields in surgery—are the source of a great amount of information. Following a large section of traumatic surgery, there are several well-illustrated pages dealing with medical evidence and evaluation of injuries suffered—a useful addition indeed.

This one-volume book covers a wide field and is well balanced. It should prove invaluable for German-speaking undergraduates, and contains numerous enough references to be useful to general practitioners.

CLINICAL APPLICATION OF HORMONE ASSAY. John A. Loraine, Edinburgh University, Scotland. 368 pp. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1958. \$5.00.

Hormone assays may be classified as chemical or biological. Dr. Loraine's experience appears to have been mainly in the field of bio-assay. He admits that chemical methods are more reliable than biological methods but technical difficulties have limited their application.

In describing bio-assay techniques, Dr. Loraine discusses briefly the chemical extraction of the hormone and then considers in more detail the biological part of the assay. The author describes clearly the degrees of precision available in the assay of each of the human hormones, and for each hormone to be assayed he recommends a method to follow. In dealing with the clinical application of hormone assays, Dr. Loraine reviews the results obtained in the more important endocrinopathies and mentions other factors that may influence these results.

It is apparent that the expense and complexity of many of the assay procedures make them prohibitive for the average medical laboratory. The field of hormone assay is in a continuous state of evolution, and refinements in technique are constantly appearing. Until further modifications in method are developed, hormone assay must remain a function of the larger medical centre.

The author's fluent style and clarity of expression should appeal to the uninitiated in the realm of biological assay as well as to the experienced investigator or clinician. This book will provide a basic reference for clinical investigators employing hormone assay for many years to come.

SELF-DESTRUCTION. A Study of the Suicidal Impulse. Beulah Chamberlain Bosselman, University of Illinois, Chicago, Ill. 94 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. \$5.25.

"A study of the suicidal impulse" is the subtitle of this little book written by a professor of psychiatry. Although clinical cases of attempted suicide are used as a starting point, the main concern of this book is with the problem of human self-destructiveness in general. It is presented in six chapters, the first three tracing the pathogenesis and development of self-destructive drives during infancy through "the death fantasies in childhood" to "gestures of suicidal attempts in adolescence". Each of these chapters has a concise introduction to developmental psychodynamics of a given maturation period with a summary discussion of pertinent literature and extensive quotations as footnotes to many pages. Secondly, individual case histories (quite intensively studied with many well-chosen verbatim quotations of patients' statements) are presented to illustrate in longitudinal perspective the psychopathology and multiple factors underlying the appearance of self-destructive drives.

Chapter 4, on the environment of loneliness, deals with statistical meanings of different sociological and cultural factors as related to suicidal drives in adults. Chapter 5, organized in the same pattern as the first three, deals with the internal motivations of adult self-destruction. The concluding chapter contains the author's summary, with some implications for prevention.

From this brief description, it becomes apparent that the author deals basically with the essentials of the problem, and she attempts to give a panoramic and synthetic view of the problem rather than to go into controversial or minute details. Dr. Bosselman uses a minimum of highly technical psychiatric terms and gives her presentation in well-understood everyday prose. Enough space is devoted to elementary facets of personality development, and this makes the book attractive to readers outside the narrow confines of psychiatric specialties. Students of psychiatric and ancillary sciences would, in the opinion of this reviewer, find this booklet valuable as a synoptic introduction and stimulus to further study of dynamics of suicidal impulse.

DISINFECTION AND STERILIZATION: THEORY AND PRACTICE. G. Sykes. 396 pp. Illust. E. & F. N. Spon Ltd., London, 1958. 75s.

This is an entirely new book on disinfection and sterilization which in an antibiotic age is still an extremely important aspect in the welfare of mankind. It deals with the theoretical and practical aspects of the subject and thus is of value to a wide group—bacteriologists, hospital staffs, industry, especially those industries concerned with large-scale disinfecting problems, public health workers and chemical engineers. It also is of value to teachers and graduate students in microbiology, chemical engineering and medicine. It is divided into six parts. Part I deals with theory of disinfection and methods of testing, part II with methods of sterilization, part III with air disinfection and sterilization, part IV with disinfection of viruses, part V with chemical disinfectants, and finally part VI with preservation and preservatives. This is a highly informative text by a leading expert in the field of industrial bacteriology.

ABSTRACTS from current literature

MEDICINE

Phenylbutazone in Treatment of Temporal Arteritis.
S. E. BJORKMAN: *Lancet*, 2: 935, 1958.

Eight case reports are presented with the diagnosis of temporal arteritis, which was verified by biopsy in three cases. Treatment with phenylbutazone (0.2 g. 3 times a day) produced prompt symptomatic relief in all cases, and there was no relapse after withdrawal of the drug. In view of the well-known striking effect of phenylbutazone on thrombophlebitis, the author believes that the effect of this drug in temporal arteritis is not only symptomatic but may possibly be due to direct action on the inflammatory process in the vessel wall. In obscure cranial symptoms in the elderly, the prompt effect of phenylbutazone may be used to aid in differential diagnosis, as illustrated by one of the cases in this report. W. GROBIN

Syndrome of Carotid Artery Insufficiency. Early Clinical Recognition and Therapy.

L. E. CREVASSE, R. B. LOGUE AND J. W. HURST: *Circulation*, 18: 924, 1958.

Carotid artery thrombosis and stenosis occurred in no less than 9.5% of one unselected autopsy series but is infrequently recognized clinically. Physicians interested in cardiovascular disease are being confronted with this syndrome because of its relationship to changes in blood pressure and cardiac output. The carotid arteries have been neglected by the pathologist, the internist and the neurologist. Careful examination and auscultation of the head and neck are rewarding in "routine strokes" and may clarify bizarre neurological symptoms in patients with cardiovascular disease. A continuous machinery murmur may be present over a partially occluded carotid, and its finding is a valuable adjunct in the early recognition of carotid artery insufficiency. Carotid artery insufficiency is a treatable disease. Its early recognition and appropriate therapy before complete thrombosis occurs will directly influence the results. S. J. SHANE

Supravalvular Aortic Stenosis.

J. J. DENIE AND A. P. VERHEUGT: *Circulation*, 18: 902, 1958.

A case is described of supravalvular aortic stenosis, suspected on clinical examination and confirmed at operation. Upon microscopical examination a muscular band was found in the left deformed cusp which showed approximately the same localization. The recorded physical signs were those of aortic valvular stenosis accompanied by those of aortic insufficiency. Sometimes the peculiar musical quality of the aortic systolic murmur was noted. Except for a loud second aortic sound, there seemed to be no physical signs that permitted a distinction between a supravalvular and a valvular stenosis. Curves obtained by retrograde left ventricular catheterization should, when examined closely, contain important clues for the diagnosis of either subvalvular or supravalvular stenosis. With the aid of aortography or selective angiocardiology, it would probably have been possible in this case to locate the site of the stenosis more accurately. S. J. SHANE

Manifestations of Rheumatic Fever after Cessation of Therapy.

E. E. FISCHER, C. W. FRANK AND M. T. BELLOWES: *Circulation*, 18: 367, 1958.

The three-week period after cessation of therapy was studied in 257 children with rheumatic fever treated for six weeks. Most patients had some manifestations of rheumatic activity, frequently an elevation of the erythrocyte sedimentation rate or of temperature. Occasionally more severe and complex manifestations occurred. The number of manifestations was greater in those patients with more severe illness on admission.

This study of the post-therapy period may provide some perspective concerning diagnostic criteria and the effectiveness of therapeutic agents in retrospect, since these manifestations of the post-therapy period are sufficiently common under apparently good conditions of management. The authors feel that study of this period should be included in attempts to define optimal therapy for rheumatic fever. S. J. SHANE

Acute Myocardial Infarction Revealed in an Isolated Premature Ventricular Beat.

K. H. KATZ, M. S. BERK AND C. I. MAYMAN: *Circulation*, 18: 897, 1958.

Two cases are reported in which the correct diagnosis of acute myocardial infarction was made possible by characteristic electrocardiographic features of infarction in isolated premature ventricular beats. These findings were present before the dominant electrocardiographic pattern became completely characteristic of the disease. It is suggested that the phenomenon here reported might be encountered more frequently as an early electrocardiographic evidence of acute myocardial infarction, if clinicians were alert to its significance. S. J. SHANE

Value of Left Heart Catheterization in Patients with Rheumatic Mitral Valve Disease.

J. F. URICCHIO *et al.*: *Dis. Chest*, 34: 525, 1958.

The value of left heart catheterization in patients with rheumatic mitral disease is discussed. Case histories are presented in which therapeutic and diagnostic problems were solved by the attainment of the ventricular filling gradient across the mitral valve. Left heart catheterization is chiefly of value in patients with rheumatic heart disease in whom marked discrepancies exist between the objective and subjective clinical picture. It also is helpful in evaluating the results of cardiac surgery and analyzing the progression of the rheumatic process after mitral commissurotomy. S. J. SHANE

Deep S Wave in Leads V₁, V₂, and V₃ in Right Ventricular Hypertrophy.

H. SHUBIN AND D. C. LEVINSON: *Circulation*, 18: 410, 1958.

The presence of a deep S wave in leads V₁ or V₂ is often interpreted as evidence suggesting left ventricular hypertrophy.

In this paper six cases are described of mitral stenosis, three of pulmonary stenosis, and one of pulmonary hypertension. In all 10 cases there was isolated right ventricular hypertrophy, and in all of them deep S waves were present in V₁, V₂ or V₃.

R/S ratios of less than 1.0 in V₁ were present in three cases. The voltage of R and V₁ was less than 0.5 millivolt in three cases. R waves were absent in aVR in three instances. S. J. SHANE

Electrocardiograms in Mitral Regurgitation.

L. G. BENTIVOGLIO *et al.*: *Circulation*, 18: 572, 1958.

The difficulty in distinguishing major mitral regurgitation from combined mitral stenosis and regurgitation by clinical methods alone is generally appreciated. Tricuspid regurgitation can also masquerade as mitral regurgitation in patients with pure mitral stenosis. For these reasons, special diagnostic studies including cardiac ventriculography and left heart catheterization must often be employed to establish more exactly the amount of obstruction and leak. Electrocardiographic reports on patients with rheumatic mitral valve disease on whom these tests are not performed, or in whom the valve is not palpated at operation, can justifiably be viewed with scepticism.

The ECG data in 65 proved cases of dynamically significant mitral regurgitation are presented. In disagreement with the current concepts and teachings, which stress the frequent occurrence and diagnostic value of left axis deviation in mitral insufficiency, this study revealed the mean manifest electric axis of ventricular activation to be either normal or deviated to the right, and electric position to be intermediate to vertical in the great majority of cases. A normal ventricular complex was present in 50% of the total series. Left ventricular hypertrophy was present in approximately 30% of the series. Combined left and right ventricular hypertrophy was encountered in only two patients, or 3% of the total group. The pattern of right ventricular hypertrophy comprised 15% of the present series.

The finding of right ventricular hypertrophy in mitral insufficiency in a relatively high number of cases is certainly unusual and in sharp contrast to the present teaching. It is important to emphasize that right ventricular hypertrophy is not an unusual feature of rheumatic mitral regurgitation. Its presence, therefore, in patients with mitral valve disease is of less value than other clinical features in the differentiation between mitral stenosis and regurgitation. S. J. SHANE

SURGERY

Pulmonary Resection for Tuberculosis under Protection of Viomycin, Promizole and Pyrazinamide.

W. R. WEBB AND K. SPARKUHL: *Dis. Chest*, 34: 484, 1958.

The temporary protection of viomycin combined with promizole or pyrazinamide in 35 pulmonary resections in 32 patients with open positive tuberculous lesions was analyzed. In each case, the tubercle bacilli were

proved or presumptively resistant to streptomycin, PAS, and isoniazid. The failure of previous medical therapy was explained by mechanical factors which would prevent cavity closure regardless of the nature or duration of medical therapy. There were four deaths unrelated to drug coverage. There has been no spread, bronchopleural fistula or empyema. Two patients had an early and one a late reactivation. Three other patients had late bacteriological relapses, but have subsequently been negative over a year. Thus, of 28 survivors followed up from six to 36 months, 22 have never shown postoperative activity and 26 have arrested or inactive disease. The authors consider that viomycin combined with either promizole or pyrazinamide offers satisfactory temporary protection for excisional surgery in tuberculosis. However, promizole has not been used since the availability of the more potent pyrazinamide. S. J. SHANE

Wounds of the Common and Internal Carotid Arteries (in French).

A. CARAYON, L. CORNET AND L. PARODI: *J. Chir.*, 76: 241, 1958.

Wounds of the carotid arteries are relatively rare in any series of vascular injuries, and many of these patients die from hæmorrhage before surgical intervention is possible. Thus a series of 20 personal cases is quite significant. These cases were collected between 1942 and 1954 in the neurosurgical centre of the French Forces in the Far East. The authors classify their series as: (1) contusions of the internal carotid artery; (2) wounds with lateral opening of the arterial lumen of the common carotid artery; (3) through and through wounds of the arterial lumen of the common carotid artery; (4) arterio-venous fistulas of the common carotid artery.

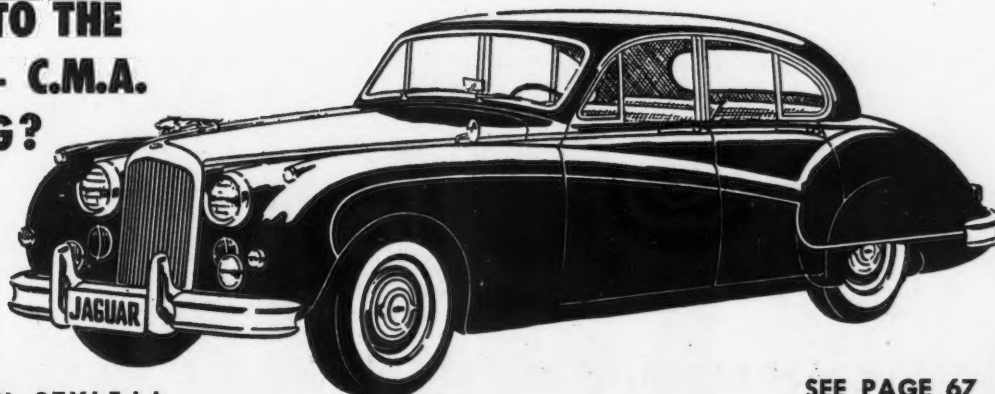
The five contusions were treated conservatively by exploration only. One patient died and three developed hemiplegia. Thrombosis of the internal carotid artery was the common sequel.

The five wounds with lateral opening of the lumen were treated by ligation of the common carotid in one case and lateral suture of the common carotid artery in another. One case with a hole in the internal carotid artery was treated by exploration only and this was followed by hemiplegia. Two other patients, treated by exploration alone, died from hæmorrhage.

The six cases of through and through wounds were treated by resection with good results in each case.

(Continued on page 497)

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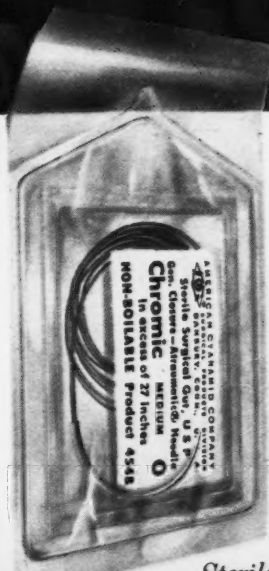
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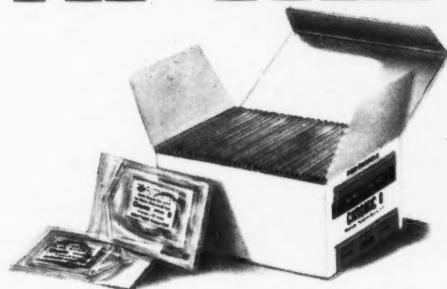
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(Continued from page 493)

In one of these cases an anastomosis was performed between the internal and external carotid arteries. In the other five cases ligature below the carotid bulb probably had the same effect.

The four arterio-venous fistulas were treated by ligature of the fistula in two cases, resection of the fistula in one, and arterial suture in the remaining case. Death occurred here from an associated medullary lesion. The otherwise good results are characteristic of these lesions, because surgery is delayed and collateral circulation has time to develop.

The test of Matas is described. Compression is carried out when the carotid has been exposed under local anaesthesia and the patient is carefully checked for any signs of cerebral ischaemia. Signs of ischaemia are an indication for preservation of the arterial blood flow, rather than ligature or resection alone. The survival time of cerebral tissue is fixed at approximately 15 minutes in the acute injury when there is presumably no collateral circulation. Hypothermia is discussed, but is impractical at present for these acute injuries. Special methods are needed for grafting or for end-to-end suture, as this cannot usually be done within a 15-minute period.

Various methods of preserving the blood flow while grafting is being carried out are discussed; the authors prefer the technique of Fryfogel of Detroit, in which a special tube is used to hold the graft into the artery while it is anastomosed at each end.

The technique of Lam and Aram, also of Detroit, involves placing a tube within the graft and threading it into the artery, above and below; temporary ligatures are applied and suturing is carried out above; below,

half of the circumference is left open. This opening is used to withdraw the tube. The remainder of the operation can then be done quickly, while the artery is clamped, thus staying well within the 15-minute time limit.

The authors do not like the technique of Shaeffer in which a polyethylene tube is employed as a bypass, or the technique of Mahorner and Spencer, which is similar. They feel that, because of the small size of the vessels in this area, the shunts do not carry sufficient blood flow to preserve adequate function.

The authors also think that the technique of Valentino, used experimentally in animals, in which a polyethylene tube is inserted through a separate window in the artery, is probably applicable to man. After the suture is completed over it, the tube is withdrawn. The artery is clamped for the short time needed to repair the hole through which the tube has been withdrawn.

T. A. McLENNAN

A New Type of Vessel-Suturing Apparatus.

K. INOKUCHI: A.M.A. Arch. Surg., 77: 954, 1958.

Suture of vessels by hand is time-consuming and irregular and very difficult in small-calibre arteries. An instrument has been developed at Kyushu University which sutures the everted ends of vessels with U-shaped steel clips. Bushings ranging in size from 2.0 to 20.0 mm. make the instrument suitable for vessels widely varying in diameter. Internal damage is less than after manual suture and there is less platelet adsorption. The risk of stenosis is also claimed to be small. The apparatus is compared with the Russian device.

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Management of Brachial-Plexus Injuries.J. F. TRACY AND E. W. BRANNON: *J. Bone & Joint Surg.*, 40-A: 1031, 1958.

Either the Duchenne-Erb or the Klumpke type of traction palsy can be caused, depending on the direction of force. Damage may occur at any level of nerve root, trunk, or division of cords of the plexus to produce paralysis, depending upon the distribution of forces. It is of course difficult, or impossible, to classify residual paralysis on the basis of nerve root injury unless the paralysis is equivalent to the loss of a peripheral nerve or a combination of peripheral nerves. The clinical correlations with the myelograms presented in this article indicate the advantages of this type of procedure in predicting the end result. Avulsion of the nerve root is of course an irreversible and irreparable injury.

Myelograms were made as early as the patient's condition would permit. Avulsion of the brachial-plexus roots was interpreted from the demonstration of the opaque oil passing through the intervertebral foramina into the traumatic diverticuli extraspinaly.

Where an avulsion of the root was demonstrated, exploration was not considered indicated. On the other hand, in cases with no demonstrable avulsion but in which it was considered that the extraspinal components of the plexus were involved, either with or without discontinuity, exploration could be considered at a later date. In cases where there is no hope of neurological repair, reconstruction measures such as shoulder or elbow arthrodesis or possibly amputation could be considered at an earlier date than would be otherwise possible. Reconstruction procedures should aim at producing shoulder stability, elbow flexibility, thumb apposition and handgrasp.

ALLAN M. DAVIDSON

THERAPEUTICS**Clinical Experience with Chlorothiazide (Diuril), with Particular Emphasis on Untoward Responses.**L. R. DINON, Y. S. KIM AND J. B. VANDER VEER: *Am. J. M. Sc.*, 236: 523, 1958.

The clinical experience of the authors with chlorothiazide as a diuretic and antihypertensive agent over a 15-month period is described in this paper. Excellent or good results were obtained in most of the 121 patients studied. Serum electrolyte disturbances were encountered in the form of the "low salt syndrome," hypochloræmic alkalosis and hypokalaemia in a number of patients. The latter finding appeared unexpectedly in certain individuals even in the absence of a marked diuresis or large doses of the drug, suggesting a selective increase in potassium excretion in some patients. Excessive hypotensive effect may occur when chlorothiazide is used concomitantly with antihypertensive drugs, especially the ganglionic blocking agents. A nearly fatal drug reaction was observed, as well as several minor side effects and one possible hæmatological toxic reaction with neutropenia and thrombocytopenia.

Electrolyte disturbances may be lessened by employing the lowest effective dosage schedule, and by a short rest period from the drug every few days. Careful clinical and laboratory observations are indicated in all patients receiving chlorothiazide, but especially in those who are also taking digitalis or antihypertensive drugs or who have serious liver disease. Supplements

of potassium chloride or citrus fruit juices are desirable in most patients.

S. J. SHANE

A Means of Lowering Elevated Blood Cholesterol Levels in Patients with Previous Myocardial Infarction.L. F. MELTZER, A. A. BOCKMAN AND G. H. BERRYMAN: *Am. J. M. Sc.*, 236: 595, 1958.

The blood cholesterol levels of 28 hypercholesterolemia patients with myocardial infarction were followed up for six months during which an unsaturated fatty acid-sitosterol-pyridoxine-vitamin E formula was added to their existing diets. The 28 patients were grouped according to their previously standardized dietary fat intakes, i.e. less than 50 g., 50-100 g., and 100 to 150 g. fat daily. The baseline cholesterol level of each patient had been well established by frequent analyses during a preliminary observation period of six to 12 months; in all cases this had remained persistently elevated; the value used was the lowest attained.

Every subject showed a decrease in baseline blood cholesterol at the end of a three-month "treatment" period of four tablespoonsful of formula daily with meals. The decrease was maintained (or additionally lowered) during a subsequent three-month "maintenance" period of two tablespoonsful of formula daily with meals. The change at the end of six months was significant for almost all. The magnitude of decrease appeared to be influenced by the amount of weight gain, but in no case was there an elevation over the original baseline level, even in the presence of a considerable gain in weight. However, the greatest blood cholesterol decline was found at low and intermediate dietary fat intakes, where weight gain was slight or absent.

S. J. SHANE

Mepacrine Therapy for Children with Petit Mal.R. A. MILLER: *Scottish M. J.*, 3: 441, 1958.

Following recent reports of the beneficial effect of mepacrine in petit mal, the author tried the effect of this drug given in smaller doses than used by previous workers but over an indefinite period. This was done in the hope of preventing the condition from becoming worse, as observed by others when treatment was stopped. Sixteen children aged 5 to 12, most of whom still had numerous petit mal attacks in spite of receiving various anticonvulsive drugs, were given 100 mg. mepacrine daily for five days each week. After periods ranging from three to 24 months, 10 patients were given additional anticonvulsive therapy in the form of meprobamate and later some of them received Tridione, the combined therapy course lasting for three to seven months. The results achieved by this treatment proved that mepacrine is of great value in petit mal either alone or in combination with another anticonvulsant. Because of the production of skin pigmentation with this dose and the appearance of grand mal attacks in two patients, the author tried one 2½-year-old girl on 50 mg. mepacrine for five days each week. On this dose her petit mal was controlled and her grand mal seizures did not become any worse. After five months on this therapy, her skin became only slightly pigmented.

W. GROBIN

(Continued on page 500)

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(Continued from page 498)

Treatment of Anticholinesterase Intoxication with Oximes.
D. GROB AND R. J. JOHNS: *Neurology*, 8: 897, 1958.

Anticholinesterase intoxication may occur after accidental exposure to insecticides such as parathion and chemical warfare gases such as sarin and on over-treating myasthenia gravis patients with octamethyl pyrophosphoramide or such drugs as neostigmine, pyridostigmine or ambenonium. Large doses of atropine ameliorate the effect of anticholinesterase on smooth muscle, secretory glands and central nervous system but have no influence on the weakness due to neuromuscular block.

The authors quote the work of Wilson and others who have been able to reverse the anticholinesterase activity of these compounds by oximes such as pyridine-2-aldoxime methiodide (2-PAM) and diacetylmonoxime (DAM). This study reports that intra-arterially administered oxime reversed the local neuromuscular block produced by anticholinesterase compounds. When administered intravenously, oxime was able to ameliorate muscular weakness produced by increasing oral or parenteral doses of anticholinesterase compounds in normal volunteers. The improvement began within 30 seconds of injection, was maximal in 5-10 minutes, and began to disappear after 20 minutes. In myasthenic patients whose strength and neuromuscular transmission had been improved by appropriate doses of anticholinesterase compound, an injection of 2-PAM or DAM reversed this effect with a return to the original state. The same reversal was observed after an overdose of anticholinesterase compounds. The authors warn that oximes should be administered cautiously to myasthenic patients given an overdose of anticholinesterase compounds, because of this return of weakness and depressed neuromuscular transmission.

W. GROBIN

Intravenous Lignocaine (Lidocaine) as an Anticonvulsant.
D. TAVERNER AND W. A. BAIN: *Lancet*, 2: 1145, 1958.

This study was designed to obtain clearcut evidence about the efficacy of intravenous lignocaine (lidocaine: Xylocaine) in status epilepticus and serial epilepsy. A double blind method was employed in which identical bottles containing lignocaine or saline were used and the effects reported in terms of prolongation of intervals between fits and the relationship between dosage of lignocaine and its action. There is evidence that lignocaine has anticonvulsant action and that this action has a linear relationship to the logarithm of the dose. In all, three patients were studied—two with focal epilepsy and one with grand mal. The authors believe that their method of study is particularly efficient in extracting maximum information from small numbers of patients, and they suggest that it could be used to assess the effects of drugs in other illnesses where signs and symptoms recur at intervals.

W. GROBIN

PUBLIC HEALTH**Effectiveness of Influenza Vaccines During an Epidemic of Asian Influenza.**B. F. GUNDELFINGER, W. T. STILLE AND J. A. BELL:
New England J. Med., 259: 1005, 1958.

3355 Navy recruits served as the population for the present study, in which 30% of the recruits received one injection of monovalent influenza (A/Japan)

vaccine, a further 30% received one injection of polyvalent A, A¹ and B vaccine, and the other 40% received an injection not containing influenza vaccine. Although the monovalent vaccine contained only 200 chick-cell agglutinating units, it proved very effective in reducing the rate of attack of febrile respiratory illness in the vaccinated as compared to the controls. It was also far more effective than the polyvalent vaccine, especially during the epidemic when there was 83-90% reduction with the former and 21-46% reduction with the latter. The protective effect became marked 10 days after inoculation. There were no side effects.

W. GROBIN

DERMATOLOGY**Multiplication of Rat-Leprosy Bacilli in Cultures of Rat Fibroblasts.**E. W. GARBUTT, R. J. W. REES AND Y. M. BARR:
Lancet, 2: 127, 1958.

Rat leprosy is studied as a model of the human disease. Until recently, neither causative organism had been cultured. Now in tissue cultures of rat fibroblasts, multiplication of rat leprosy bacilli is reported by the authors.

ROBERT JACKSON

Skin Fragments Removed by Injection Needles.T. GIBSON AND W. NORRIS: *Lancet*, 2: 983, 1958.

When a needle is thrust through skin it commonly cores out a fragment of tissue. In a series of 300 tests with a wide range of needles the frequency of this occurrence was 69%. There is no great variation in the frequency with different sizes of needles, but the skin fragment is roughly proportional to the size of the lumen. Side-opening needles and those with a fitted stylet do not remove skin fragments. The skin fragment removed may plug the needles, be aspirated into the syringe, or be ejected into the patient's subcutaneous or muscular tissues or into the peripheral venous system. The possibility of introduction of pathogenic organisms into the tissues and lungs via the small skin fragments is discussed.

ROBERT JACKSON

PÆDIATRICS**Pathogenesis and Treatment of Kernicterus (in German).**H. KELLNER AND J. STOERMER: *Deutsche med. Wchnschr.*, 83: 1983, 1958.

In recent years many workers have been able to prove that the pigment responsible for the colouring of basal ganglia and other areas of the brain in kernicterus is identical with indirect bilirubin. The nature of direct and indirect bilirubin has been elucidated; the difference between the two lies in the coupling with glucuronic acid. This coupling occurs in the liver and to a lesser degree in the kidneys. Hepatic bilirubin results from esterification of two molecules of glucuronic acid with two propionic acid remnants of a molecule of bilirubin. This coupling makes the bilirubin water-soluble and enables it to be excreted through the kidneys. Indirect bilirubin is supposed to be transported in the blood in colloidal suspension and is soluble in alcohol, after which it will react with the diazo reagent.

(Continued on page 502)

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(Continued from page 500)

Indirect bilirubin has a great affinity for the cells of the basal ganglia, which are rich in lipoids.

Kellner and Stoermer quote investigations by Zetterström and Ernster demonstrating that indirect bilirubin is cytotoxic, causing inhibition of phosphorylation and of the vital oxidation processes within cells. They admit that there is so far no absolute evidence that the icteric staining of the basal ganglia is the cause of the clinical picture called kernicterus. It may be postulated that indirect bilirubin is attracted by already damaged portions of the brain and the staining is thus a secondary phenomenon, but this does not negate the fact that elevation of bilirubin level in the first week of life is a potential danger to the infant whose liver is not yet able to detoxify it efficiently. Periston N (polyvinylpyrrolidone 30-40 c.c. intravenously) given daily for 7-10 days has been used by Kellner and Stoermer for all infants with icterus gravis for the past two years, together with an exchange transfusion.

The success of this treatment was further enhanced when daily doses of adrenocortical extract were added to the treatment. Lately, this treatment has also been used for infants with potential or threatening kernicterus, and the extract has been routinely given to all premature infants. After two years of this prophylactic treatment for kernicterus, the authors feel justified in stating that the clinical picture of kernicterus has become a rarity; when it occurs, its symptoms disappear rapidly (in 1-2 days) when Periston is added to the regimen. The improvement in the clinical picture is paralleled in these cases by a disappearance of the jaundice. Another approach to the treatment of kernicterus would be to utilize the fact that bilirubin is converted into biliverdin on exposure to ultraviolet irradiation, thus losing its cytotoxic properties. The authors quote Cremer, Perryman and Richards, who have succeeded in lowering the bilirubin content of the blood of infants with icterus neonatorum by exposing them to short-wave light. W. GROBIN

INDUSTRIAL MEDICINE

Influence of Clothing on Pattern and Severity of Burns in Colliery Fire-Damp Ignitions.

M. N. TEMPEST AND J. B. ATKINS: *Brit. J. Indust. Med.*, 15: 147, 1958.

Although it is recognized that a large proportion of deaths from domestic burns are associated with ignition of clothing, little emphasis has been laid on the problem in industry. Recently experience in four underground gas ignitions in British coal mines has drawn attention to the role of unsuitable clothing as a major factor in determining the outcome of these disasters. Evidence derived from study of the 66 men affected is reviewed in detail. Reference is made to information in literature.

The material for study consisted of detailed records of the extent, distribution and severity of the burned areas, together with necropsy findings in most of the 28 fatal cases. Consideration was given also to the clothing worn by each man. Other information was obtained by questioning the patients and other witnesses. The opinion of the Inspector of Mines was sought as regards extent of exposure in terms of duration and probable temperatures.

Analysis of the findings led to certain conclusions:

Clothing has a valuable protective function, but the clothing now commonly worn by miners is liable to ignite. This leads to complication of the original primary burns, especially of upper parts of the body, to additional risk of burns of the hands and forearms, to probable increase of burns of the respiratory tract, and to possible risk of carbon monoxide poisoning. Burned clothing remaining in close proximity to the skin can produce deep burns.

Safer clothing than that now usually worn by miners could reduce the risk of serious injury by burning in these colliery accidents. It should satisfy two requirements: (1) So far as possible, all vulnerable areas should be protected. The following items are recommended—gloves, a shirt or vest with sleeves, preferably elbow-length, and a properly designed helmet, which will not easily become dislodged. (2) All outer garments should possess a high degree of resistance to ignition. Three solutions are suggested—use of naturally resistant fabrics such as wool or wool and nylon mixture (which avoids danger from static electrical charges); use of textiles rendered "flame-proof" by an acceptable chemical process; use of a flame-resistant rinse after laundering. The first and second ways appear to offer the most satisfactory solutions.

MARGARET H. WILTON

Prolonged Intensive Occupational Exposure to DDT.

M. F. ORTELEE: *A.M.A. Arch. Indust. Health*, 18: 433, 1958.

Investigations of the acute toxicity of DDT for man have been limited to a few experimental studies and to a small number of accidents. The present report discusses the effects in a group of 40 men whose exposure had been intensive and prolonged. They were employed by three firms engaged in the manufacture and/or formulation of DDT. Exposure was mainly dermal and respiratory.

Information concerning their ages, length of exposure, amount and type of exposure, job description, exposure rating, and urinary excretion of DDA, is presented together with results of clinical examinations and laboratory tests. The latter included (1) complete medical history, using the Cornell Medical Index Health Questionnaire; (2) physical and neurological examination; (3) haemoglobin determination (Haden-Hauser haemoglobinometer); (4) white blood cell count and differential; (5) sulfobromophthalein test (dose of 5 mg./kg. and blood specimen after 45 minutes); (6) plasma and erythrocyte cholinesterase determination; (7) urinary DDA excretion.

Analysis of the findings showed no correlation between DDT exposure and the frequency and distribution of abnormalities, with the exception of the urinary excretion of DDA and a few cases of minor skin and eye irritation. The skin irritations were mild. The eye irritations were associated with high concentrations of DDT dust, but were not severe enough to interfere with work or to induce the men to wear goggles.

The author concludes that, with the possible exception of rare hypersensitivity reactions, it is unlikely that any illness or symptom complex identifiable as chronic DDT poisoning would be caused by DDT at the current dietary level. MARGARET H. WILTON



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MEDICAL NEWS in Brief

(Continued from page 468)

**A NEW DERIVATIVE
OF ISONIAZID**

A special issue of the Italian medical journal, *Minerva Medica* (49: December 8, 1958), is entirely devoted to experimental and clinical contributions on a Japanese derivative of isoniazid; this is furyl-2-methyl-ketone isonicotinylhydrazone. The drug is said to be less toxic than isoniazid and free

of side effects in therapeutic doses. In one series of 15 patients with chronic cavitary tuberculosis, previously treated with disappointing results by older anti-tuberculosis drugs, the new derivative was given in daily doses of 5 mg. per kg. body weight for two or three months. The drug was well tolerated, and clinical and radiological results were excellent. The patients felt well and improved in general condition; sputum frequently became negative and cavi-

ties diminished in size with loss of fluid levels and marked diminution in shadows between lesions. Sedimentation rate and blood findings were favourably affected. In four other series, each containing 16 to 31 patients, similar results were obtained.

**INSTITUTE ON
MEDICAL TEACHING**

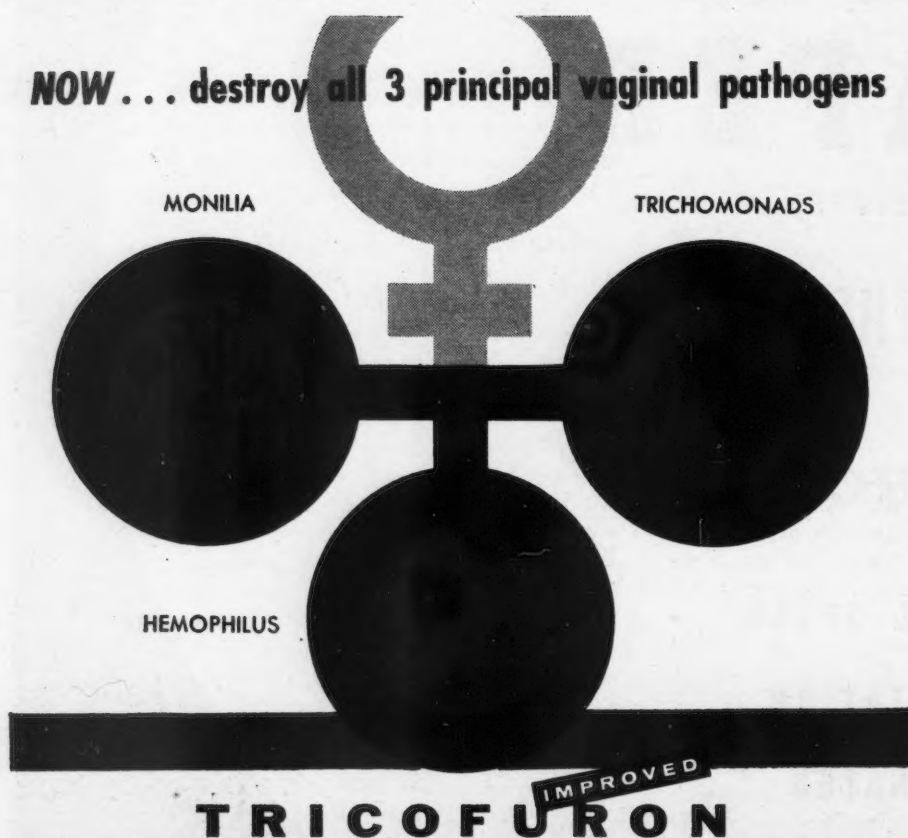
The Second Summer Institute on Medical Teaching jointly sponsored by the University of Buffalo and the Association of American Medical Colleges will be held in Buffalo, June 9-18, 1959. The Institute will provide an opportunity for medical instructors to join with education specialists in an examination of teaching and learning in medical schools. Included in the presentations, demonstrations and discussions led by University of Buffalo teachers from the Schools of Medicine, Education and Arts and Science will be such topics as the nature of learning; the nature of medical students and medical faculties; the philosophical background for higher education in the United States; the use of lecture and laboratory, ward exercise and clinical conference as well as less familiar methods of instruction; the use of tests and other appraisal devices for measuring student performance in a medical school. Opportunity for consultation on individual instructional problems will also be provided.

Attendance at the Institute will be limited. Interested members of Medical School faculties in the United States and Canada may apply for registration or further information by writing to: Dr. George E. Miller, Associate Professor of Medicine, University of Buffalo School of Medicine, Buffalo 14, New York.

**INTERNATIONAL
CONGRESS OF
INTERNAL MEDICINE**

The 6th International Congress of Internal Medicine will be held in Basel, Switzerland, August 24-27, 1960. This Congress will be organized in conjunction with the Swiss Society for Internal Medicine. For further details, apply to the Secretariat of the 6th International Congress of Internal Medicine, 13, Steinentorstr., Basel.

(Continued on page 58)

NOW... destroy all 3 principal vaginal pathogens

Vaginal Suppositories and Powder

TRICOFURON is a new, powerful, broad-spectrum antifungal and antiparasitic agent. It is effective against all three principal vaginal pathogens: Monilia, Trichomonads, and Hemophilus. Tricofuron is a derivative of isoniazid, which has been found to be highly effective against these organisms. It is a white, crystalline powder that is easily absorbed and acts quickly to destroy the pathogens. Tricofuron is safe for use and does not cause irritation or discomfort. It is available in both suppository and powder form for easy administration. Tricofuron is a new breakthrough in the treatment of vaginal infections. It is a powerful, broad-spectrum agent that is effective against all three principal vaginal pathogens. It is a white, crystalline powder that is easily absorbed and acts quickly to destroy the pathogens. Tricofuron is safe for use and does not cause irritation or discomfort. It is available in both suppository and powder form for easy administration. Tricofuron is a new breakthrough in the treatment of vaginal infections.

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Suppositories: Each contains 100 mg. of Tricofuron. Insert 1 suppository into the vagina at bedtime for 7 days.

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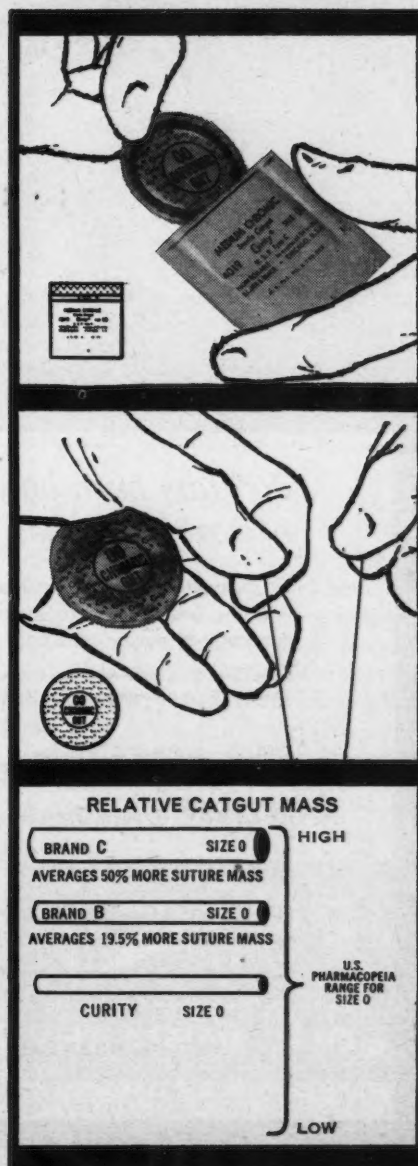
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The smallest suture—with the greatest strength. Size for size, the average strand of new Curity Catgut is smaller in diameter than any other surgical gut. Smaller sutures mean less tissue reaction.

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MEDICAL NEWS in brief

(Continued from page 56)

**KARTAGENER'S TRIAD:
A FAMILY STUDY**

Kartagener's triad, the coexistence of bronchiectasis, situs inversus and sinusitis, has been reported by several workers as occurring in more than one member of a family. Gorham and Merselis (*Bull. Johns Hopkins Hosp.*, 104: 11, 1959) describe two cases of this syndrome in siblings whose family tree was studied through four generations. Detailed history of 29 members, of whom nine were

also examined and x-rayed, failed to reveal any other cases of Kartagener's triad. In most cases a reliable history is sufficient to rule out the presence of this condition, as the majority of patients with it seek medical attention and their symptoms usually appear in childhood and persist. Respiratory complaints predominate, as can be seen from a review of 38 cases reported in the literature since 1950. There were only two instances in which respiratory symptoms became troublesome as late as the end of the third decade of life, and 90% of patients reviewed by Bergstrom

developed severe respiratory complaints before the age of 14.

**PARENTERAL MAG-
NESIUM SULFATE
THERAPY IN CORONARY
DISEASE**

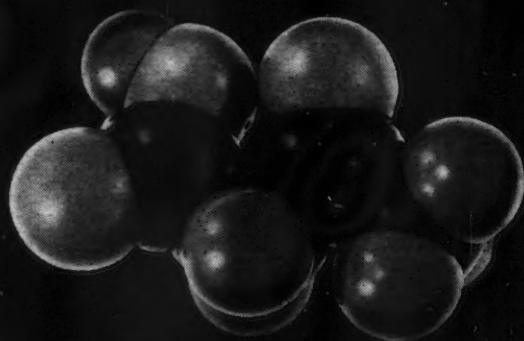
Malkiel-Shapiro (*South African M. J.*, 32: 1211, 1958) has used magnesium sulfate therapy in acute attacks of coronary thrombosis and in angina pectoris for the past 23 years. Two years ago, he published a preliminary report on the value of this treatment, and the present paper summarizes his experience and quotes the results of others who have used magnesium sulfate in coronary heart disease. In acute cases of myocardial infarction, the only contraindication to this treatment is shock. None of the patients under 70 treated with magnesium sulfate in an attack of coronary thrombosis during some 23 years died; the only patient who died moribund when treatment was started. The first dose should not exceed 0.5 ml. of 50% magnesium sulfate, which the author gives intramuscularly. Other writers prefer the intravenous route which is more hazardous although possibly more effective. The second dose is given 12-24 hours later and injections are repeated on the 4th, 7th, 10th and 14th day. Heparin and all other accepted forms of treatment are used concurrently. In angina pectoris, 12 injections of 0.5-2 ml. of 50% magnesium sulfate are administered at five-day intervals. This course is repeated every 4-6 months, or else continuous therapy by weekly injections is given. Although experimental and laboratory findings support this therapy (Selye is reported to have found that magnesium salts are effective in preventing artificially produced infarct-like lesions in the rat's myocardium), it is admitted that the rationale of the treatment is obscure. Adding up the reported statistics of five workers who used this treatment in angina, shows that 66% of the patients experienced prolonged or lasting remission of pain.

CAT-SCRATCH FEVER

Collipp and Koch (*New England J. Med.*, 260: 278, 1959) have recently reported a case of cat-
(Continued on page 61)

AN AMES CLINIQUICK

CLINICAL BRIEFS FOR MODERN PRACTICE

*do "fats burn only in the fire
of carbohydrates"?*

No. Actually, the normal intermediate products of fat metabolism—ketone bodies from the liver—are oxidized in the cells independently of glucose oxidation.

Source—Hoffman, W. S.: *The Biochemistry of Clinical Medicine*, Chicago, The Year Book Publishers, Inc., 1954, pp. 96, 97.

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MEDICAL NEWS in brief (Continued from page 58)

scratch fever associated with an osteolytic lesion. The patient, a four-year-old boy, had pain in the right knee associated with low-grade fever. A history of contacts with cats, a maculopapular rash and the presence of an aseptic lymphadenitis together with a positive cat-scratch skin test served to establish the diagnosis. A roentgenogram revealed an osteolytic lesion in the right femoral intertrochanteric area with slight periosteal reaction along the medial aspect. Material removed through a needle biopsy contained several granulomas with central necrosis surrounded by epithelioid cells and lymphocytes. Progressive healing took place over the next five months.

DISSECTING ANEURYSMS OF THE CAROTID ARTERY AFTER ARTERIOGRAPHY

In two patients, reported by Ross Fleming and Park (*Neurology*, 9: 1, 1959), dissecting aneurysm developed after arteriography. A 58-year-old man was subjected to arteriography six weeks after subarachnoid haemorrhage. The injection of dye into the right carotid artery caused considerable pain in the right ear, and on the next day transient blindness in the right eye and right-sided headache developed. During the next 48 hours drowsiness and complete left hemiplegia supervened. On surgical exposure of the right carotid arteries, restoration of internal carotid circulation was produced by resection of the occluded portion of the internal, external and common carotid arteries and end-to-end anastomosis. A subintimal haematoma was found in the wall of the common carotid artery and a mural thrombus on the opposite wall. The patient died 18 hours later, and at autopsy marked swelling and softening of the right cerebral hemisphere was found.

In the second patient, who died at the age of 32 of a massive intracerebral haematoma, a percutaneous carotid arteriogram was done 12 hours before death. There was some difficulty in introducing the needle into the artery, which was punctured several times. At autopsy a small dissecting aneurysm

of the common carotid artery was an incidental finding, and the cause of death was severe cerebral swelling associated with temporal and cerebellar pressure cones following operative removal of a large intracerebral haematoma.

Photographs and photomicrographs show clearly the traumatizing effect of multiple needle punctures and their association with the subintimal haemorrhage and dissection. The need for careful technique, especially when injecting arteries already made friable by atheroma, and for awareness of this rare but real risk

in patients subjected to arteriography, are stressed.

POSTGRADUATE DIPLOMAS AND COURSES IN THE UNITED KINGDOM

The Commonwealth Medical Advisory Bureau of the British Medical Association has produced a new version of its "Summary of Regulations for Postgraduate Diplomas and of Courses of Instruction in Postgraduate Medicine". This is a valuable document for

(Continued on page 64)

Which type of Hearing Aid is best for your patient?

If this were your patient's audiogram, which type of hearing aid would you recommend? It is taken from the case history of a 32-year-old bookkeeper whose hearing loss was diagnosed, at age 19, as otosclerosis, with little or no perceptive component. In consultation with his doctor, the patient decided against surgical intervention.

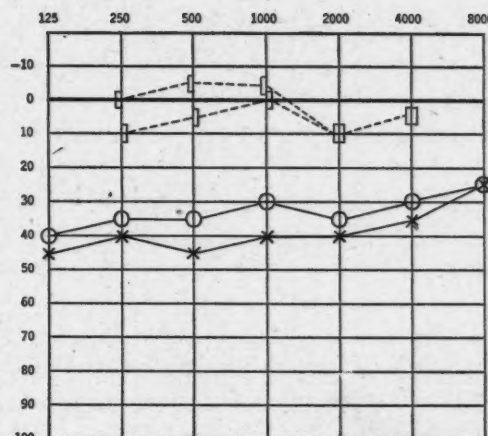
This report is but one of many typical cases described in a new book, prepared especially for the medical profession by the Hearing Aid Division of Zenith Radio Corporation.

Clinical Findings: Ave. loss, R: 33 db, L: 42 db, B.B.A.: 33 db, SRT: 35 db, MCL: 55 db, TD: 100 db. Discrimination: L: 92%, R: 94%.

Prognosis: Patient should adapt readily to moderate gain hearing aid, air conduction type.

Recommendations: Any of these five Zenith Hearing Aids: Zenith "Citation" or "Challenger" Eyeglass Hearing Aid. At-the-ear Zenith "Diplomat" with L-1 earphone, or "Ambassador." Moderate gain conventional Zenith Hearing Aid — "Crusader" model in "M" tone setting.

Now Ready for Doctors ... a valuable reference book designed to help you recommend the right type of hearing



aid for your patients. Besides the actual typical case history outlined above, Zenith's new book, "Which Type of Hearing Aid for Your Patient," describes many other cases, and lists the appropriate Zenith Hearing Aid. Also contains a complete description of all types of Zenith Hearing Aids and their uses. For your free copy, write to: Zenith Radio Corporation of Canada, Dept. C11PC, 1470 "The Queensway" Toronto, Ontario.



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With ARISTOCORT there has been freedom from sodium and water retention, absence of potassium depletion, psychic equilibrium is rarely disturbed, a low incidence of peptic ulcer and a low incidence of osteoporosis with compression fracture.

Indications: Rheumatoid arthritis, bronchial asthma, perennial rhinitis, other respiratory allergies, psoriasis, other inflammatory and allergic dermatoses, disseminated lupus erythematosus, nephrotic syndrome, pulmonary emphysema and fibrosis, palliation in neoplastic diseases such as the leukemias and lymphomas.

Supplied: 1 mg. scored tablets (yellow); 2 mg. scored tablets (pink); 4 mg. scored tablets (white).



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MEDICAL NEWS in brief

(Continued from page 61)

physicians wishing to undertake study in the United Kingdom, for it lists all the postgraduate diplomas available, together with the requirements for entry to courses, the times of examinations and the fees required. It also lists postgraduate courses in the United Kingdom which are unrelated to diplomas. Copies of this document are stated to be available in many centres in Canada, including the Faculties of

Medicine of the Canadian medical schools, and the pathology departments of the Vancouver General Hospital, the City Hospital, Calgary, the City Hospital, Saskatoon, and St. Boniface Hospital, Winnipeg. Registrars of the various Colleges of Physicians and Surgeons across Canada have also been provided with copies.

BAHAMAS CONFERENCES

The following Bahamas Conferences are announced: Seventh

Bahamas Medical Conference, March 30-April 11, 1959. Eighth Bahamas Medical Conference, November 27-December 17, 1959. Second Bahamas Surgical Conference, December 28, 1959-January 16, 1960. Second Bahamas Serendipity Conference, January 17-January 30, 1960. Ninth Bahamas Medical Conference, April 1-April 14, 1960. All conferences will be held at the British Colonial Hotel, Nassau, Bahamas. For further information, contact Dr. B. L. Frank, Organizing Physician, Bahamas Conferences, P.O. Box 4037, Fort Lauderdale, Fla.

AMERICAN DRUG INDEX

In 1957 a most useful little book appeared entitled "The American Drug Index".* The latest annual edition for 1959 is now available, and continues the useful work of its predecessors. An alphabetical listing of drugs and preparations with extensive cross-indexing, it gives generic, brand, chemical and official synonyms. Dosage and use are indicated and combinations of certain preparations are indexed together. In spite of the plethora of new drugs, the authors have managed to reduce the size of the new volume by over 40 pages.

*American Drug Index 1959. Prepared by C. O. Wilson and T. E. Jones. 671 pp. J. B. Lippincott Company, Philadelphia and Montreal, 1959. \$5.75.

RESULTS OF SURGICAL CORRECTION OF ATRIAL SEPTAL DEFECT

Uncomplicated atrial septal defect is an indication for operation in all patients between the ages of 2 and 45 years. The preoperative assessment of the patient's condition is based mainly on the history and physical examination. Fluoroscopy is helpful, the electrocardiogram is usually abnormal and cardiac catheterization provides important information. This latter procedure was used by Blount *et al.* (J. A. M. A., 169: 210, 1959) as an aid in diagnosis in 83 out of 100 patients, but is not performed any more unless there is need for clarifying some unusual features in a given case.

Of the 100 patients 38 were asymptomatic and 10 severely incapacitated. Only eight patients gave a history indicating conges-

(Continued on page 67)

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"...represents a significant decrease in the period of disability for the patient. No specific or multiple vitamin preparations have proved as beneficial as the use of [Protamide]."

— Richard T. Smith
MEDICAL CLINICS OF
NORTH AMERICA

HERPES ZOSTER

"Protamide is a valuable remedy in the treatment of herpes zoster. It is helpful in relief of pain and apparently aids in involution of the cutaneous lesions."

— Frank C. Combes, et. al.
NEW YORK STATE JOURNAL
OF MEDICINE

RADICULITIS

"Protamide provided fast relief for the type of cases of neuritis which had proved intractable to Vitamin B₁, B₁₂ and physical therapy...it is now our therapy of choice..."

— Henry W. Lehrer, et. al.
NORTHWEST MEDICINE

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"...it is certain we have obtained more satisfactory results with Protamide than with those drugs previously employed such as the neurodrugs, antibiotics, vitamins, ACTH and corticosteroids."

— Prof. F. Caramazza
ITALIAN JOURNAL OF
OPHTHALMOLOGY

HERPES ZOSTER

"...Protamide is of definite value in the relief of pain in herpes zoster. Further, vesicles and crusts disappear much more rapidly than in untreated cases."

— William C. Marsh
U. S. ARMED FORCES
MEDICAL JOURNAL

NEURITIS

"Protamide is deemed a safe drug...with the ability to control 80.7 per cent of patients with radiculitis of posterior roots believed due to virus infection."

— Richard T. Smith
NEW YORK MEDICINE

A folio of these and other reprints
available on request.

Sherman Laboratories

Windsor, Ontario

MEDICAL NEWS in brief

(Continued from page 64)

tive failure. There were seven post-operative deaths which occurred among the first 43 cases. Eighty-one patients are considered cured and an additional three are clinically cured, although investigations still show left-to-right shunt at the atrial level. Two patients have been troubled by postoperative arrhythmia but one of them is improving. One patient still shows some breathlessness on exertion but is gradually improving and one 33-year-old housewife who had marked pulmonary hypertension before operation shows no regression of the vascular changes but claims that she is feeling better. In their total experience with this operation in 125 cases, the authors had no additional deaths after the first 43 operations and feel that in the relatively asymptomatic child 2-10 years of age the operation carries less than 2% mortality.

THE PORPHYRIAS

Present-day knowledge of the porphyrias has produced the following classification of its various forms: (1) congenital, (2) acute and (3) "porphyria cutanea tarda". In the rare mixed forms a combination of skin lesions with abdominal and neurological and mental manifestations is present. Canivet and Fallot (*Deutsche med. Wchnschr.*, 84: 63, 1959) have studied 43 cases of porphyria during the past 10 years; three were of the congenital type and occurred in three siblings (two male and one female) out of 10 born to the same parents during 1931-1951. Red discoloration of the urine was observed on the first day of life in all three, and sensitivity to light developed at the age of 3. High porphyrin levels in the urine were present at all times. During the 10 years under observation the patients have never complained of abdominal or neurological symptoms, but they are underdeveloped and have various dystrophies of skin, fingers and ears. Alopecias and disorders of joints and tendons are also present.

Acute porphyria was observed in 17 patients, of whom 13 had abdominal and nervous symptoms, one had abdominal and mental symptoms and three had latent porphyria. Ten of these patients have since died, demonstrating dramati-

cally how serious the prognosis of this disease is. Two of the latent cases were found in close relations of known porphyria patients and the other was discovered accidentally. All 22 patients with the cutaneous form, which is the most frequent form encountered in France, had a remarkable degree of similarity to each other. None of them showed familial incidence in spite of a careful search for latent cases among relatives. The average age of onset of symptoms was 49 years with a range of 33 to

66 years. Photosensitivity of lesser intensity than in acute porphyria and without dystrophies dominated the clinical picture, and there were no abdominal or central nervous system disturbances present. Other skin lesions included microcysts, atrophic spots and pigmentation. Alcoholism was present in 17 of these cases and hepatomegaly of some degree was found in 16 patients. The prognosis is considerably better than in acute porphyria, and 21 of the 22 patients are still

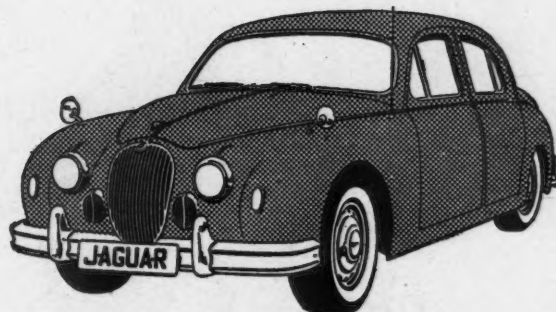
(Continued on page 74)

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MEDICAL NEWS in brief
(Continued from page 67)

alive, some even showing regression of the disorder. Porphobilinogen was not found in any of these patients. The only case of mixed porphyria occurred in a 14-year-old boy who had skin lesions at the age of eight. The following year he had abdominal symptoms which led to removal of a normal appendix. The following years were characterized by alternating abdominal and central nervous system symptoms, such as headaches and emotional instability. During one year he again experienced photosensitivity of the skin but for the past few years has had only symptoms relating to the nervous system. The authors point out that with very few exceptions all the cases reported in the world literature can be easily classified as one or other of the forms described above. The late cutaneous form in particular appears to be a well-defined form with its characteristic clinical picture and course.

—
**INTERNATIONAL
MEDICAL CONFERENCE
ON MENTAL
RETARDATION**

The preliminary program of the First International Medical Conference on Mental Retardation, to be held at the Eastland Hotel, Portland, Maine, July 27-31, 1959, is now to hand. Contributors will include specialists from the United States, Germany, Austria, France, and England and subjects discussed will include: brain anatomy and mental retardation, the autonomic nervous system and brain activity, enzymes and brain activity, metabolic defects in relation to mental retardation, congenital malformations of the central nervous system, infections and mental retardation, mongolism, erythroblastosis, medical and surgical treatment of mental retardation, childhood schizophrenia and mental retardation as part of the training program in child psychiatry. Simultaneous interpretation will be available; there will be a scientific and commercial exhibition; films will be available and a program of social activities is planned. Further information from Dr. Ella Langer, State of Maine Department of Health and Welfare, Augusta, Maine.

**NOSE-BLEEDING AND
HIGH BLOOD PRESSURE**

Two groups of patients were reviewed by Mitchell (*Brit. M. J.*, 1: 25, 1959) in order to test the validity of the statement that nose-bleeding is often associated with high blood pressure. In the first group the records of 173 patients attending a hypertension clinic and 201 patients known to have a diastolic pressure of more than 100 mm. Hg were examined for

occurrence of nose bleeding. Of the 17 patients who had complained of epistaxis, this had been the presenting symptom in eight and had led to the discovery of hypertension. Another 17 had had gastro-intestinal bleeding; in only three could a lesion be found to account for this. A second group of 162 patients admitted to the E.N.T. department because of nose-bleeding included 132 patients without nasal disease. Of them, 64

even
when
other therapy
fails

in
eczemas
dermatoses
ulcers
burns
pruritus (ani et vulvae)
slow healing wounds
diaper rash
chafing
etc.

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patients had a diastolic pressure over 95 mm. Hg. These findings support the statement that nose-bleeding in the absence of nasal disease is associated with high blood pressure.

PARENTS WHO DEMAND TONSILLECTOMY

All pædiatricians are familiar with the parents who insist on having their child's tonsils and

adenoids removed, although the grounds for the insistence are not apparent. Furman (*J. Pediat.*, 54: 195, 1959) discusses ways in which the pressure to perform this operation may be counteracted. He feels that one of the main reasons for tonsil surgery in children is pressure from the parents, and that this stems from two popular misconceptions about tonsils: (1) that the only function of the tonsils is to be removed surgically; (2) that

any respiratory illness is a tonsillitis. Parents should be told that the tonsils have a purpose, that the child can get along nicely even if it keeps its tonsils, and that not every attack of tonsillitis is an indication for operation.

Furman stresses that the time to educate the parents is when the first question about the tonsils is raised. Later on, they may have become emotionally involved and be feeling guilty that they have neglected their child by not having a tonsillectomy done.

Parents will also insist on tonsillectomy out of a sense of angry frustration over symptoms which have nothing to do with the tonsils, such as anorexia, insomnia or constant irritability of the child. Having failed to deal with the child's complaints, the parents switch to an area where successful activity is possible. Moreover, parents will often claim later that the operation has cleared such conditions as enuresis, anorexia or behaviour problems. What has of course been changed is the parents' attitude towards the child.

AMERICAN HEART ASSOCIATION

The 1959 Annual Meeting and Scientific Sessions of the American Heart Association will be held on October 23-27 in Philadelphia. The Scientific Sessions are scheduled for October 23-25 at the Trade and Convention Center. The Annual Meeting of the National Assembly, delegate body representing all program interests and geographical areas of the Association, will be held in the Hotel Bellevue Stratford, October 26-27.

A deadline of June 12 has been set for submission of abstracts of papers to be presented at the Scientific Sessions and applications for space for scientific exhibits. Official forms for submitting abstracts and space applications for scientific exhibits may be obtained from Dr. F. J. Lewy, Assistant Medical Director, American Heart Association. Applications for space for industrial exhibits may be requested through Steven K. Herlitz, Inc., 280 Madison Avenue, New York 16, N.Y.

Inquiries concerning hotel reservations and the Assembly meetings may be addressed to William F.

(Continued on page 80)



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MEDICAL NEWS in brief
(Continued from page 75)

McGlone, Secretary, American Heart Association, 44 East 23rd Street, New York 10, N.Y.

RENAL CONCENTRATION
IN HEAVY EXERCISE

According to a recent report by Raisz, Au and Scheer (*J. Clin. Invest.*, 38: 8, 1959), heavy exercise impairs renal concentrating ability in hydropenic normal man. An experiment was carried out on

eight volunteers who abstained from drinking any fluid for about 20 hours before the test, and exercised by running up and down three flights of stairs for 30 minutes. In other instances they were required to step up and down a 17-inch step every three seconds, also for a period of 30 minutes. In the latter instance the subjects were receiving at the same time an infusion of normal saline with 100 μ g. of vasopressin and, in other cases, of 5% mannitol and 0.36% saline solution intravenously flowing at either slow or fast rates.

In the heavy exercise without solute loading, there was an abrupt decrease in urine flow, osmolar clearance and sodium excretion to less than half the pre-exercise values, with a gradual return to pre-exercise levels by the third or fourth hour. Creatinine clearance and potassium excretion also diminished and returned to normal slightly sooner than the other values. When heavy exercise was carried out during solute loading, an abrupt decrease in urine flow, osmolar clearance and electrolyte excretion was also observed although all values rapidly returned to pre-exercise levels. These effects could not be prevented by the administration of vasopressin and are therefore considered not to be the consequence of a decrease in endogenous antidiuretic hormone production.

Several mechanisms for impairment of concentrating ability are suggested by these experimental results. According to the authors, perhaps the simplest mechanism would be impairment due to reduction of the supply of oxygen to the active transport system at the concentrating site. Another could be the reduced flow rate in Henle's loops which could impair the hair-pin countercurrent mechanism for concentrating the fluid in these loops. A third possibility is offered by the slowing of blood flow through renal medullary capillaries which could impair concentrating ability if these vessels provide the only means for returning water reabsorbed from the collecting ducts to the circulation.



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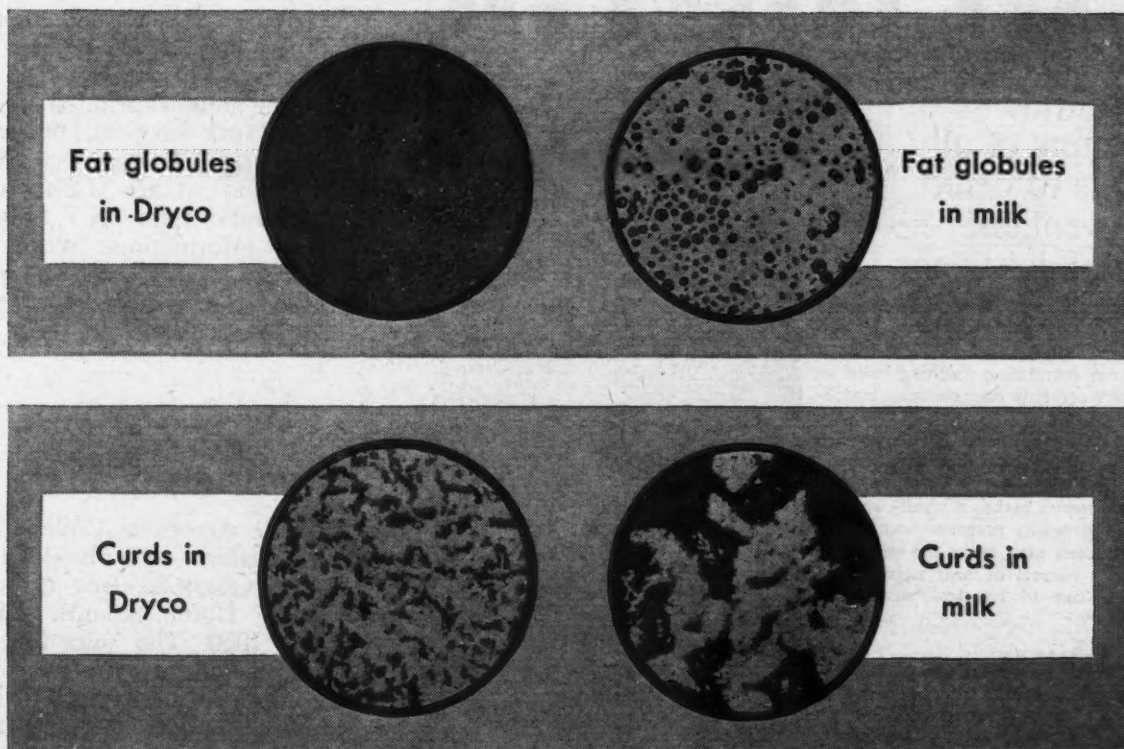
HYPERLIPÆMIA
IN ACUTE
GLOMERULONEPHRITIS

Over the last 10 years Heymann and Wilson of Western Reserve University School of Medicine (*J. Clin. Invest.*, 38: 186, 1959) investigated 111 unselected cases of acute glomerulonephritis with a view to establishing the level of serum proteins, cholesterol and total lipids. All of these cases were proven by the usual clinical and laboratory diagnostic criteria and 75% of the patients were older than four years of age whereas it is known that in nephrosis the majority of children are younger than four years of age. The values obtained were compared with

(Continued on page 90)

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MEDICAL NEWS in brief

(Continued from page 81)

others from 123 patients admitted to hospital for various ailments. All these controls were free of renal complications and were well nourished. Serum protein and albumin values of the nephritic group were below the lowest values obtained in the controls in over 20% of cases. A mild to moderate degree of hypercholesterolaemia was noted in 40% of children suffering from acute glomerulonephritis, and an elevation of total serum lipids was found in 43%. The authors point

out that the finding of markedly increased serum cholesterol or total lipid values should no longer exclude the diagnosis of acute glomerulonephritis. Greater emphasis should be placed on bacteriological and serological tests in the diagnosis of this disease.

CONGRESS ON ACUPUNCTURE

The Tenth International Jubilee Congress of Acupuncture will be held at the Domus Medica, 60 Blvd. Latour Maubourg, Paris 7,

France, on May 9, 10 and 11, 1959. The congressional theme will be rheumatic diathesis and acupuncture.

The Congress Headquarters handling all scientific questions is at 8 Avenue Franklin D. Roosevelt, Paris 8. All applications for housing and travel at the Congress should be sent to Agence Univers, 9 Boulevard des Capucines, Paris 2, France.

INTERNATIONAL COLLEGE OF SURGEONS

The 24th Annual Congress of the North American Federation, International College of Surgeons, will be held in Chicago, September 13-17, 1959. The federation is composed of the United States, Canadian, Mexican, and Central American sections.

The 12th biennial International Congress of the International College of Surgeons will be held in Rome, Italy, May 15-18, 1960. For information write to the Secretariat, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

The annual spring meeting of the New York Surgical Division, International College of Surgeons, will be held at the Concord Hotel, Kiamesha Lake, N.Y., May 28-30. For information, write to Dr. Milton S. Weinberg, chairman of arrangements, 37-41 75th Street, Jackson Heights 72, N.Y.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The American College of Chest Physicians will hold its Silver Anniversary meeting at the Ambassador Hotel, Atlantic City, June 3-7, 1959. The scientific program will include prominent speakers on all aspects of heart and lung diseases. In addition to formal presentations, there will be a number of symposia, round table luncheon discussions, postgraduate seminars, and motion pictures. At the Fireside Conferences, inaugurated in 1955, more than 60 experts in chest disease will lead discussions on topics of current interest.

Examinations for Fellowship in the College will be held on Thursday, June 4, and on Thursday

(Continued on page 92)

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(1) Baird, H. W., III: J. Pediat. 52:715, 1958. (2) Centerwall, W. R.: J.A.M.A. 165:392 (Sept. 28) 1957. (3) Wright, S. W.: J.A.M.A. 165:2079 (Dec. 21) 1957. (4) Kretschmer, N., and Eitzwiler, D. D.: Pediatrics 21:445, 1958. (5) Sanford, A. H.: Postgrad. Med. 23:A-68 (May) 1958. (6) Berry, H. K.; Sutherland, B.; Guest, G. M., and Warkany, J.: J.A.M.A. 167:2189 (Aug. 30) 1958. Available: PHENISTIX Reagent Strips—Bottles of 50.



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MEDICAL NEWS in brief*(Continued from page 90)*

evening more than 200 new Fellows will receive their certificates of Fellowship at the Convocation. The Presidents' Banquet and annual dance will take place on Saturday, June 6.

To commemorate the Silver Anniversary, the College is publishing a history of the growth of the organization since its first meeting in 1935.

A.M.A. ADVICE ON 1959 PUBLIC RELATIONS PROGRAMS

In the January 1959 issue of *The PR Doctor* issued by the Public Relations Department of the American Medical Association, a priority list of subjects for medical society public relations programs is given. First on the list comes the financing of medical care for the patient over 65, a burning issue in the States at the moment in view of government interest in this field. Medical societies are urged to establish committees on aging which will work closely with public relations committees and community groups. Secondly, societies are urged to keep in mind that many of the long-range goals of medical public relations will be realized by the enactment of legislation. They are therefore advised to invite their government representatives to a society meeting during the year to discuss forthcoming bills in the medical field, and to keep in constant touch with the legislatures to let them know the societies' views. Thirdly, the A.M.A. offers to supply any interested medical society in the States with a complete set of materials helping them to expose the fallacies in nutrition and food faddism. A drive is also to be conducted by the A.M.A. in conjunction with the U.S. Public Health Service and the National Safety Council this spring to promote the use of seat-belts in automobiles. The proper treatment of athletic injuries is suggested as another point at which medical societies could co-operate with athletic coaches and school administrators. *PR Doctor* suggests that medical societies might also take some time to re-evaluate their grievance committees and disciplinary structure, in order to see whether it is giving

good service and whether the public is aware of the service it has to offer.

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DISORDERED PUL- MONARY FUNCTION IN MITRAL STENOSIS

Preliminary investigations by MacIntosh *et al.* (*Ann. Int. Med.*, 49: 1294, 1958) indicated that the oxygen ventilatory equivalent—that is, the volume of air breathed per litre of oxygen consumed bears an inverse relationship to exercise tolerance. The present study measured the oxygen ventilatory equivalent and explored its relationship with pulmonary diffusing capacity in patients with mitral stenosis. The studies were performed before commissurotomy and in some cases were repeated in the postoperative period. The oxygen ventilatory equivalent was found to be elevated in the more severe cases of mitral stenosis and rose progressively with the severity of the disease. Decrease in oxygen ventilatory equivalent consistent with the clinical improvement was observed in the majority of patients following commissurotomy. In patients with reduced exercise tolerance, impairment of diffusion was demonstrated preoperatively, and no improvement of the diffusing capacity was observed during the 3-16 months after operation. The decrease of hyperventilation and lack of improvement in diffusing capacity indicates that there is no direct relationship between the two.

The authors believe that their results indicate that the oxygen ventilatory equivalent determined during exercise provides an objective and accurate assessment of pulmonary function in these patients.

ANATOMY OF THE MOUTH

A very readable and comprehensive account of the gross anatomy of the mouth has been prepared by Dr. J. F. Huber, professor and head of the department of anatomy, Temple University School of Medicine, Philadelphia, for the latest of the Ciba Clinical Symposia. The article carries a magnificent series of illustrations done by the well-known Dr. Netter.